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FILE COVERS 1907 - 1 Apr 2002  VOL 136 ISS 14
FILE LAST UPDATED: 30 Mar 2002  (20020330/ED)

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and/or SDIs in the H/Z/CA/CAplus files incorporating CAS Registry
Numbers with the P indicator executed between 12/27/01 and 1/23/02 may
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=>
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=> d stat que l2
L1            32 SEA FILE=REGISTRY ABB=ON  PLU=ON  TPDINPAWYXXRGIRPVGRFXX|SRAHQH
                 SMEIRTPDINPAWYAGRGIRPVGRF|TPDINPAWYAGRGIRPVGRF|SRAHQHSMETRTPDIN
                 PAWYTGRGIRPVGRF|TPDINPAWYTGRGIRPVGRF|SRTHRHSMEIRTPDINPAWYASRGIR
                 PVGRF|TPDINPAWYASRGIRPVGRF/SQSP
L2            25 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L1


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L2   ANSWER 1 OF 25  HCAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         2001:619131  HCAPLUS
DOCUMENT NUMBER:          135:327590
TITLE:                    Expression of prolactin-releasing peptide in human
                          placenta and decidua
AUTHOR(S):                Yasui, Yumiko; Yamaguchi, Masaaki; Jikihara, Hiroaki;
                          Yamamoto, Toshiya; Kanzaki, Toru; Murata, Yuji
CORPORATE SOURCE:         Department of Specific Organ Regulation, Osaka
                          University Graduate School of Medicine, Osaka,
                          565-0871, Japan
```

SOURCE: Endocrine Journal (Kyoto, Japan) (2001), 48(3), 397-401
CODEN: ENJOEO; ISSN: 0918-8959
PUBLISHER: Japan Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The aims of this study were to det. whether the human placenta and decidua express PRL-releasing peptide (PrRP) mRNA and whether PrRP regulates PRL secretion from cultured human decidual cells. PrRP gene expression was analyzed by reverse transcription (RT)-PCR, and the level of the gene expression was quantified by a RNase protection assay. PrRP gene expression was detected in both the placenta and decidua. These tissues expressed PrRP mRNA throughout pregnancy and the level of PrRP mRNA expression somewhat increased during midpregnancy. Placental and decidual cells also expressed PrRP mRNA, in vitro. To det. whether PrRP affects decidual PRL secretion, human endometrial stromal cells and decidual cells were cultured and treated with or without 1 .mu.M PrRP31. PrRP31 did not affect PRL secretion in either short or long term incubation. Moreover, the RT-PCR anal. indicated that human decidua does not express the PrRP receptor, hGR3, mRNA. These findings suggest that PrRP produced by the human placenta and decidua does not affect decidual PRL secretion due to a lack of the receptor, and that it may play other roles during pregnancy.

IT 209466-89-7
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(prolactin-releasing peptide expression in human placenta and decidua)

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 25 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:473667 HCAPLUS
DOCUMENT NUMBER: 135:175761

TITLE: A novel function of prolactin-releasing peptide in the control of growth hormone via secretion of somatostatin from the hypothalamus

AUTHOR(S): Iijima, Norio; Matsumoto, Yoshio; Yano, Takahiko; Tanaka, Masaki; Yamamoto, Takanori; Kakihara, Kenshi; Kataoka, Yuko; Tamada, Yoshitaka; Matsumoto, Hirokazu; Suzuki, Nobuhiro; Hinuma, Shuji; Ibata, Yasuhiko
CORPORATE SOURCE: Departments of Anatomy and Neurobiology, Kyoto Prefectural University of Medicine, Kyoto, 602-0841, Japan

SOURCE: Endocrinology (2001), 142(7), 3239-3243
CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The present study examd. a novel function of PRL-releasing peptide (PrRP) on the neuroendocrine system. PrRP-immunoreactive nerve fibers and nerve terminals were located in the vicinity of the somatostatin (SOM)-neurons in the hypothalamic periventricular nucleus (PerVN). Immuno-electron microscopy revealed that PrRP-immunoreactive nerve terminals made synaptic contacts with nonimmunoreactive neuronal elements in the PerVN. Intracerebroventricular (icv) administration of PrRP induced immediate early gene, NGFI-A, in SOM-neurons in the PerVN. Double-labeling in situ hybridization showed that some parts of SOM-neurons in the PerVN expressed PrRP receptor mRNA. Therefore, some parts of SOM-neurons in the PerVN are considered to be directly innervated by PrRP via PrRP receptor. In addn. to the above morphol. characteristics, icv administration of PrRP

decreased plasma GH levels. Such inhibitory effects of PrRP on the secretion of GH from the anterior pituitary were diminished by depletion or neutralization of SOM. From these findings it was strongly suggested that SOM-neurons respond to PrRP and secrete SOM into the portal vessels and thus inhibit GH secretion from the anterior pituitary.

IT **215510-06-8**, rat prolactin-releasing peptide 31
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(prolactin-releasing peptide regulation of growth hormone secretion mediation by somatostatin release from hypothalamus and mechanisms thereof)

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 3 OF 25 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:380420 HCAPLUS
DOCUMENT NUMBER: 135:14693
TITLE: Use of peptide
INVENTOR(S): Kitada, Chieko; Matsumoto, Hirokazu; Hinuma, Shuji
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 90 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001035984	A1	20010525	WO 2000-JP8119	20001117

W: AE, AG, AL, AM, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MA, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 1999-327900 A 19991118
JP 2000-297073 A 20000926

AB A ligand and a peptide having an effect of regulating the secretion of CRH which are useful as CRH secretion regulating agents or analgesics in ameliorating, preventing and treating various diseases concerning the CRH secretion such as hypoaldosteronism, hypocortisolemia, secondary and chronic hypoadrenocorticism, Addison's disease (boredom, nausea, pigmentation, hypogonadism, hair removal, hypotension), adrenal gland hypofunction and obesity. The CRH secretion regulating agent is a G protein-coupled receptor ligand.

IT **192526-83-3 192526-94-6 192527-01-8**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; corticotropin-releasing hormone secretion regulating agent for treating hypoaldosteronism, hypocortisolemia, secondary and chronic hypoadrenocorticism, Addison's disease, adrenal gland hypofunction and obesity)

IT **191919-77-4 191919-78-5 191919-81-0 191919-84-3 192588-09-3 192588-12-8**
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(corticotropin-releasing hormone secretion regulating agent for treating hypoaldosteronism, hypocortisolemia, secondary and chronic hypoadrenocorticism, Addison's disease, adrenal gland hypofunction and obesity)

IT **192588-10-6 192588-11-7 192588-13-9**
192588-14-0 192588-15-1 192588-16-2
215662-83-2
RL: PRP (Properties)
(unclaimed protein sequence; use of peptide)

IT **191919-79-6 191919-80-9 191919-82-1**
191919-83-2 191919-85-4 191919-86-5
RL: PRP (Properties)
(unclaimed sequence; use of peptide)

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 4 OF 25 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:113528 HCAPLUS
DOCUMENT NUMBER: 135:191115
TITLE: Isolation and characterization of the rat prolactin-releasing peptide gene: multiple TATA boxes in the promoter region
AUTHOR(S): Yamada, Masanobu; Ozawa, Atsushi; Ishii, Sumiyasu; Shibusawa, Nobuyuki; Hashida, Tetsu; Ishizuka, Takahiro; Hosoya, Takeshi; Monden, Tsuyoshi; Satoh, Teturou; Mori, Masatomo
CORPORATE SOURCE: First Department of Internal Medicine, Gunma University School of Medicine, Maebashi, Gunma, 371-8511, Japan
SOURCE: Biochemical and Biophysical Research Communications (2001), 281(1), 53-56
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The prolactin-releasing peptide (PrRP) gene is a novel bioactive peptide expressed in very restricted regions in the brain. To explore the mol. mechanism of PrRP gene expression, we cloned and characterized the gene and its promoter region. The gene spans approx. 2.4 kb and contains three exons and two introns. 3'RACE anal. showed that a polyadenylation signal 103 bp downstream from the stop codon was functional. Primer extension anal. indicated three transcriptional start sites (TSSs) 92, 199, and 325 bp upstream from the translational start site. Interestingly, in addn. to the putative binding sites for SP1-1, AP-2, and Oct-2A, three characteristic TATA boxes were identified close to these TSSs. Transient transfection study using a series of deletion mutants revealed that the middle TATA box is important for the promoter activity. Furthermore, the cloned 1.6 kb promoter region was active only in neuron- and pituitary-derived cell lines, and the promoter region -1600.apprx.-800 bp worked as a neg. regulatory element. We demonstrated for the first time, the genomic organization and promoter function of the PrRP gene, and this knowledge will facilitate elucidation of transcriptional control of the PrRP gene. (c) 2001 Academic Press.

IT **192526-94-6**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; isolation and characterization of the rat prolactin-releasing peptide gene)

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 5 OF 25 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:101186 HCAPLUS
DOCUMENT NUMBER: 134:142305
TITLE: Prolactin-releasing peptide and method for regulating autonomic functions and treating pain
INVENTOR(S): Panula, Pertti Aarre Juhani; Pertovaara, Antti; Kalso, Eija; Korpi, Esa
PATENT ASSIGNEE(S): Oy Juvantia Pharma Ltd., Finland
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001009182	A1	20010208	WO 2000-FI664	20000803

W: CA, JP, US
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.: US 1999-365756 A 19990803
US 2000-531567 A 20000320

AB The present invention relates to a method for regulating autonomic functions, such as blood pressure, and further to a method for treating pain by prolactin-releasing peptide (PrRP) or through its receptor. This peptide regulates blood pressure and pain mechanisms, and is expressed in complementary areas with neuropeptide FF (NPFF). Specific antisera developed against the N- and/or C-terminal domains of PrRP may be used for diagnostics.

IT 209466-90-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PrRP20; methods for regulating autonomic functions and treating pain using C-terminal fragments of prolactin-releasing factor)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 6 OF 25 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:855347 HCAPLUS
DOCUMENT NUMBER: 134:66407
TITLE: Involvement of prolactin-releasing peptide in the preovulatory luteinizing hormone and prolactin surges in the rat
AUTHOR(S): Hizume, Takatoshi; Watanobe, Hajime; Yoneda, Masashi; Suda, Toshihiro; Schioth, Helgi B.
CORPORATE SOURCE: Third Department of Internal Medicine, Hirosaki University School of Medicine, Hirosaki, Aomori, 036-8562, Japan
SOURCE: Biochemical and Biophysical Research Communications (2000), 279, 35-39
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Prolactin (PRL)-releasing peptide (PrRP) is a novel hypothalamic peptide

reported as a potent and specific stimulator of PRL secretion. In this study, the authors examd. a possible role of PrRP in the ovarian steroid-induced PRL surge in the rat, simultaneously observing the change in LH surge. Expts. were performed on both normally-fed and three-day-fasted rats, which were ovariectomized and primed with estradiol and progesterone. From 11:00 to 18:00 h, blood was collected every 30 min to measure LH and PRL. All the following substances were given intracerebroventricularly at 11:00 h. Compared to control serum, anti-rat PrRP31 serum caused a significant redn. of the LH and PRL surges. The antiserum also delayed the onset of PRL surge. Fasted rats were devoid of significant surges of the hormones, while 3.0, but not 0.5 nmol of rat PrRP31 given to these animals produced a significant recovery of PRL surge. Although LH surge was not reinstated, basal LH secretion was transiently stimulated by 3.0 nmol of PrRP31. These results demonstrate for the first time a significant participation of PrRP in the preovulatory LH and PRL surges in the rat. Possible indirect pathways mediating this effect of PrRP were discussed, in view of the unique anatomical distribution of PrRP in the hypothalamus. (c) 2000 Academic Press.

IT 215510-06-8, Rat prolactin-releasing peptide-31
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(prolactin-releasing peptide involvement in ovarian steroid induced preovulatory LH and prolactin surges in rat)

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 7 OF 25 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:824291 HCAPLUS
DOCUMENT NUMBER: 134:21425
TITLE: Protection of endogenous therapeutic peptides from peptidase activity through conjugation to blood components
INVENTOR(S): Bridon, Dominique P.; Ezrin, Alan M.; Milner, Peter G.; Holmes, Darren L.; Thibaudeau, Karen
PATENT ASSIGNEE(S): Conjuchem, Inc., Can.
SOURCE: PCT Int. Appl., 733 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000069900	A2	20001123	WO 2000-US13576	20000517
WO 2000069900	A3	20010215		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
WO 2000070665	A2	20001123	WO 2000-IB763	20000517
WO 2000070665	A3	20010419		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,				

IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1105409 A2 20010613 EP 2000-936023 20000517
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

EP 1171582 A2 20020116 EP 2000-929748 20000517
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.: US 1999-134406P P 19990517
US 1999-153406P P 19990910
US 1999-159783P P 19991015
WO 2000-IB763 W 20000517
WO 2000-US13576 W 20000517

AB A method for protecting a peptide from peptidase activity in vivo, the peptide being composed of between 2 and 50 amino acids and having a C-terminus and an N-terminus and a C-terminus amino acid and an N-terminus amino acid is described. In the first step of the method, the peptide is modified by attaching a reactive group to the C-terminus amino acid, to the N-terminus amino acid, or to an amino acid located between the N-terminus and the C-terminus, such that the modified peptide is capable of forming a covalent bond in vivo with a reactive functionality on a blood component. The solid phase peptide synthesis of a no. of derivs. with 3-maleimidopropionic acid (3-MPA) is described. In the next step, a covalent bond is formed between the reactive group and a reactive functionality on a blood component to form a peptide-blood component conjugate, thereby protecting said peptide from peptidase activity. The final step of the method involves the analyzing of the stability of the peptide-blood component conjugate to assess the protection of the peptide from peptidase activity. Thus, the percentage of a K5 kringle peptide (Pro-Arg-Lys-Leu-Tyr-Asp-Lys-NH2) conjugated to human serum albumin via MPA remained relatively const. through a 24-h plasma assay in contrast to unmodified K5 which decreased to 9% of the original amt. of K5 in only 4 h in plasma.

IT **192588-09-3 192588-12-8 309255-64-9**
RL: PRP (Properties)
(unclaimed protein sequence; protection of endogenous therapeutic peptides from peptidase activity through conjugation to blood components)

IT **191919-78-5 191919-81-0 191919-84-3**
RL: PRP (Properties)
(unclaimed sequence; protection of endogenous therapeutic peptides from peptidase activity through conjugation to blood components)

L2 ANSWER 8 OF 25 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:785176 HCAPLUS
DOCUMENT NUMBER: 134:13518
TITLE: Characterization of the binding of [125I]-human prolactin releasing peptide (PrRP) to GPR10, a novel G protein coupled receptor
AUTHOR(S): Langmead, Christopher J.; Szekeres, Philip G.; Chambers, Jonathan K.; Ratcliffe, Steven J.; Jones, Declan N. C.; Hirst, Warren D.; Price, Gary W.; Herdon, Hugh J.
CORPORATE SOURCE: Department of Neuroscience Research, SmithKline

Beecham Pharmaceuticals, Essex, CM19 5AW, UK
SOURCE: British Journal of Pharmacology (2000), 131(4), 683-688
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB GPR10 is a novel G-protein coupled receptor that is the human orthologue of rat Unknown Hypothalamic Receptor-1 (UHR-1). Human prolactin-releasing peptide (PrRP) has been identified as an endogenous ligand for GPR10, and occurs as 31 and 20 amino acid forms. The present study characterizes the binding of [125I]-PrRP-20 to HEK293 cells stably expressing GPR10 receptors. Specific binding of [125I]-PrRP-20 was saturable, and anal. suggested evidence of both high and low affinity sites, with KD values of 0.026 and 0.57 nM resp., and Bmax values of 3010 and 8570 fmol mg protein-1 resp. Kinetic studies were unable to distinguish two sites, but single site anal. of assocn. and dissocn. data produced a KD of 0.012 nM. Competition studies revealed that human and rat PrRP-20 and PrRP-31 all display high affinity for GPR10. A range of other drugs which are known ligands at receptors which share limited homol. with GPR10 were also tested. None of the drugs tested, including the RF-amide neuropeptide FF, demonstrated any affinity for GPR10. Human PrRP-20 failed to alter basal or forskolin-stimulated levels of intracellular cAMP in HEK293-GPR10 cells, suggesting that GPR10 does not couple via either Gs or Gi. Functional studies using measurements of intracellular calcium confirmed that human and rat PrRP-20 and PrRP-31 are all potent, full agonists at the GPR10 receptor. The response was blocked both by thapsigargin, indicating mobilization of intracellular Ca2+ stores. These studies indicate that [125I]-PrRP-20 is a specific, high affinity radioligand for GPR10. The availability of this radioligand binding assay will be a valuable tool for the investigation of the key features involved in PrRP binding and studies on the localization and function of GPR10.

IT **215510-22-8D**, Human Prolactin releasing peptide, derivs., iodine 125-labeled
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(prolactin releasing peptide characterization as radioligand for GPR10 G protein coupled receptor)

IT **215510-22-8**, Human prolactin releasing peptide
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(prolactin releasing peptide characterization as radioligand for GPR10 G protein coupled receptor)

IT **215510-06-8**, Rat Prolactin-releasing peptide-31
222988-10-5, Rat Prolactin-releasing peptide-20
235433-36-0, Human PrRP-20
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(prolactin releasing peptide characterization as radioligand for GPR10 G protein coupled receptor)

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 9 OF 25 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:456901 HCAPLUS
DOCUMENT NUMBER: 133:79323
TITLE: peptide for ameliorating, preventing and treating

	various diseases relating to the oxytocin secretion
INVENTOR(S):	Matsumoto, Hirokazu; Kitada, Chieko; Hinuma, Shuji
PATENT ASSIGNEE(S):	Takeda Chemical Industries, Ltd., Japan
SOURCE:	PCT Int. Appl., 71 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	Japanese
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000038704	A1	20000706	WO 1999-JP7199	19991222
W: AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CR, CU, CZ, DM, EE, GD, GE, HR, HU, ID, IL, IN, IS, KG, KR, KZ, LC, LK, LR, LT, LV, MA, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
JP 2000191696	A2	20000711	JP 1998-369585	19981225
EP 1142580	A1	20011010	EP 1999-961301	19991222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.:	JP 1998-369585	A	19981225
	WO 1999-JP7199	W	19991222

AB The invention relates to use of a polypeptide recognized as a ligand by a G protein-coupled receptor protein. Because of having an effect of promoting the secretion of oxytocin, this ligand polypeptide is useful as a drug for ameliorating, preventing and treating various diseases relating to the oxytocin secretion such as week pains, atonic bleeding, before or after expulsion of placenta, uterine recovery failure, etc.

IT **192526-83-3**, Protein (cattle clone pBOV3 G protein-coupled receptor ligand)
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(amino acid sequence; peptide for ameliorating, preventing and treating various diseases relating to the oxytocin secretion)

IT **191919-77-4 191919-78-5 191919-81-0 191919-84-3 192588-09-3 192588-12-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peptide for ameliorating, preventing and treating various diseases relating to the oxytocin secretion)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 10 OF 25 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:	2000:310598 HCAPLUS
DOCUMENT NUMBER:	133:53944
TITLE:	Prolactin-releasing peptides do not stimulate prolactin release in vivo
AUTHOR(S):	Jarry, Hubertus; Heuer, Heike; Schomburg, Lutz; Bauer, Karl
CORPORATE SOURCE:	Abteilung fur Klinische und experimentelle Endokrinologie, Universitat Gottingen, Hannover,

D-30625, Germany
SOURCE: Neuroendocrinology (2000), 71(4), 262-267
CODEN: NUNDAJ; ISSN: 0028-3835
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The prolactin (PRL)-releasing activity of the novel prolactin-releasing peptides (PrRPs) was studied in vivo using male and lactating female rats. Whereas TSH-releasing hormone effectively stimulated PRL and TSH release as expected, PrRP in both animal models neither stimulated PRL secretion nor affected the release of other pituitary hormones. At the anterior pituitary level, in situ hybridization (ISH) histochem. and Northern blot anal. revealed significantly higher expression levels of PrRP receptor (UHR-1) transcripts in female compared to male rats but not between lactating and nonlactating animals. By ISH, expression of UHR-1 mRNA was also detected in the intermediate lobe but not in the posterior pituitary. UHR-1 transcripts were also readily detectable in various hypothalamic brain areas, whereas expression of PrRP mRNA was restricted to the ventral part of the dorsomedial hypothalamic nucleus but was not detected in neuroendocrine hypothalamic nuclei (e.g., PVN, SON). The authors thus assume that in the central nervous system, PrRP may likely have functions as a neuromodulatory. However, together with the detailed cytochem. studies of various investigators that failed to detect PrRP-immunopos. nerve endings in the median eminence, the authors' results strongly suggest that the hypothalamic PrRPs cannot be classified as hypophysiotropic factors.

IT **215510-06-8**, Rat prolactin-releasing peptide 31
2229B8-10-5, Rat prolactin-releasing peptide 12-31
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(prolactin-releasing peptides do not stimulate prolactin release in vivo)

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 11 OF 25 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:210499 HCAPLUS
DOCUMENT NUMBER: 132:260688
TITLE: GPR10 as a target for identifying weight modulating compounds
INVENTOR(S): Stricker-Kongrad, Alain; Gu, Wei
PATENT ASSIGNEE(S): Millennium Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000017641	A1	20000330	WO 1999-US21243	19990922

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,

DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6197530	B1	20010306	US 1998-172353	19981014
AU 9960421	A1	20000410	AU 1999-60421	19990922
EP 1116032	A1	20010718	EP 1999-969494	19990922
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2001010921	A1	20010802	US 2001-799955	20010306

PRIORITY APPLN. INFO.: US 1998-101380P P 19980922
US 1998-172353 A1 19981014
WO 1999-US21243 W 19990922

AB The invention features assays for the identification of modulators of body wt. useful for the treatment of obesity and cachexia. The methods of the invention involve cell-free and cell-based assays that identify compds. which bind to and/or activate or inhibit the activity of GPR10, a G protein-coupled receptor, followed by an in vivo assay of the effect of the compd. on feeding behavior, body wt., or metabolic rate. The invention also features compds. which bind to and/or activate or inhibit the activity of GPR10 as well as pharmaceutical compns. comprising such compds. In addn., the invention includes nucleic acid mols. comprising a nucleotide sequence encoding all or a portion of murine GPR10, polypeptides comprising all or a portion of murine GPR10, antibodies directed against murine GPR10, and animals harboring a murine GPR10 transgene (e.g., mice overexpressing murine GPR10).

IT **215510-06-8**
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BPR (Biological process); PRP (Properties); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(GPR10 as target in screening of modulators of body wt., feeding behavior or metabolic rate)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 12 OF 25 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:142155 HCAPLUS
DOCUMENT NUMBER: 132:274519
TITLE: A novel action of the newly described prolactin-releasing peptides: cardiovascular regulation
AUTHOR(S): Samson, W. K.; Resch, Z. T.; Murphy, T. C.
CORPORATE SOURCE: Department of Pharmacological and Physiological Sciences, St. Louis University School of Medicine, St. Louis, MO, USA
SOURCE: Brain Res. (2000), 858(1), 19-25
CODEN: BRREAP; ISSN: 0006-8993
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The physiol. relevance of the recently described prolactin-releasing peptides (PrRPs) has yet to be established. Here, we demonstrate the low potency of the PrRPs (min. ED: 100 nM), compared to that obsd. for TSH-releasing hormone (TRH, min. ED: 1.0 nM), to stimulate prolactin (PRL) release from cultured pituitary cells harvested from lactating female rats. Anat. studies question the role of these peptides in neuroendocrine control of lactotroph function. Instead, peptide and peptide receptor mapping studies suggest potential actions in hypothalamus and brainstem unrelated to the control of anterior pituitary hormone secretion. Intracerebroventricular (i.c.v.) administration of both PrRP-20 and PrRP-31 (0.4 and 4.0 nmol) resulted in significantly increased mean

arterial blood pressure in conscious, unrestrained rats [peak elevations vs. baseline: PrRP-20, 10% and 16%, low and high dose peptide; PrRP-31, 7% and 10%; compared to the response to 0.1 nmol angiotensin II (A II), 15-17%]. Similar doses of peptide did not significantly alter water drinking in response to overnight fluid deprivation, or thirst or salt appetite in response to an isotonic hypovolemic challenge. Thus, the effect on blood pressure appeared relatively specific. We suggest that these peptides, identified originally as ligands for a receptor found in abundance in pituitary gland, play a broader role in brain function and that the ability of them to stimulate PRL release may not represent their primary biol. function.

IT **215510-06-8**, Rat prolactin-releasing peptide 31
222988-10-5
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(prolactin-releasing peptides intracerebroventricular administration elevation of arterial blood pressure in rats)

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 13 OF 25 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:769263 HCAPLUS
DOCUMENT NUMBER: 132:59425
TITLE: Anatomical distribution of prolactin-releasing peptide and its receptor suggests additional functions in the central nervous system and periphery
AUTHOR(S): Roland, Barbara L.; Sutton, Steven W.; Wilson, Sandy J.; Luo, Lin; Pyati, Jayashree; Huvar, Rene; Erlander, Mark G.; Lovenberg, Timothy W.
CORPORATE SOURCE: R. W. Johnson Pharmaceutical Research Institute, San Diego, CA, 92121, USA
SOURCE: Endocrinology (1999), 140(12), 5736-5745
CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A recently identified neuropeptide with PRL-releasing capabilities binds to and activates a previously known orphan G protein-coupled receptor, GPR10. We initiated a study to define the pharmacol. of the peptide/receptor interaction and to identify the distribution of the peptide and its receptor in the central nervous system to elucidate sites of action of the peptide. The PRL-releasing peptide (PrRP) is a C-terminally amidated, 31-amino acid peptide derived from a 98-amino acid precursor. Radioiodinated PrRP-(1-31) binds to its receptor with high affinity (1 nM) and stimulates calcium mobilization in CHOK1 cells stably transfected with the receptor. A series of N-terminal deletions reveals that the PrRP-(12-31) amino acid is equipotent to PrRP-(1-31). Further N-terminal deletions reduce the affinity of the ligand considerably, although PrRP-(25-31) is still able to compete for binding and behaves as an agonist. The arginine residues at position 26 and 30 are crit. for binding, as substitution with either lysine or citrulline reduces the affinity substantially. In situ hybridization reveals a distinct tissue distribution for both the peptide and receptor mRNAs. The receptor is expressed abundantly in the reticular thalamic nucleus, periventricular hypothalamus, dorsomedial hypothalamus, nucleus of the solitary tract, area postrema, anterior pituitary, and adrenal medulla. The peptide mRNA is expressed in the dorsomedial hypothalamus, nucleus of the solitary tract, ventrolateral reticular nucleus, and intestine. This tissue distribution suggests an alternative function of PrRP than its purported

hypophysiotropic function, such as a potential role for PrRP in the central feedback control of neuroendocrine and autonomic homeostasis. Further work using selective agonists and antagonists should help define addnl. physiol. roles of this novel mammalian neuropeptide.

IT **215510-22-B**, Human prolactin-releasing peptide **235433-36-0**, 12-31-Human prolactin-releasing peptide
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); PRP (Properties); BIOL (Biological study); PROC (Process)
(prolactin-releasing peptide and prolactin-releasing peptide receptor distribution in central nervous system and periphery and structure-activity relations therefor)

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 14 OF 25 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:753334 HCAPLUS
DOCUMENT NUMBER: 132:11632
TITLE: Monoclonal antibody to ligand 19P2 and its therapeutical use
INVENTOR(S): Matsumoto, Hirokazu; Kitada, Chieko; Hinuma, Shuji
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9960112	A1	19991125	WO 1999-JP2650	19990520
W: AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9937331	A1	19991206	AU 1999-37331	19990520
JP 2000037187	A2	20000208	JP 1999-140305	19990520
EP 1081222	A1	20010307	EP 1999-919662	19990520
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: JP 1998-140293 A 19980521
WO 1999-JP2650 W 19990520

AB Provided is a mouse IgG-type monoclonal antibody (in particular, P2L-1Ca) highly reactive to ligand 19P2 and being capable of neutralizing the arachidonic acid metabolite-releasing activity of ligand 19P2. Thus, the antibody can be used as a diagnostic, prophylactic, or therapeutic agent for various diseases assocd. with the ligand 19P2-assocd. pituitary function regulatory mechanism (e.g., promotion of the prolactin secretion), the central nerve regulatory mechanism, the pancreatic function regulatory mechanism, etc. Furthermore, the monoclonal antibody can be used for the detn. of ligand 19P2 or its derivs. by the sandwich immunoassay, esp. by using the antibody recognizes the middle portion of the ligand. This assay method is useful for the study of the physiol. functions of ligand 19P2 and its deriv. Prepn. of antigenic fragments of human, rat, and bovine ligand 19P2; prepn. of IgG-type mouse monoclonal antibodies P2L-1Ca and P2L-2Ca to ligand 19P2; and use of the monoclonal

antibodies for the detn. of ligand 19P2 by sandwich-EIA were demonstrated.

IT **191919-77-4P**
RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(bovine ligand 19P2 fragment (residues 1-31) as antigen; monoclonal antibody to ligand 19P2 and therapeutical use)

IT **192588-15-1P 215510-22-8P**
RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(human ligand 19P2 fragment (residues 1-31) as antigen; monoclonal antibody to ligand 19P2 and therapeutical use)

IT **191919-78-5P**
RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(human ligand 19P2 fragment (residues 12-25) as antigen; monoclonal antibody to ligand 19P2 and therapeutical use)

IT **191919-B1-0P 191919-84-3P**
RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(human ligand 19P2 fragment (residues 12-31) as antigen; monoclonal antibody to ligand 19P2 and therapeutical use)

IT **1925BB-09-3P**
RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(rat ligand 19P2 fragment (residues 1-31) as antigen; monoclonal antibody to ligand 19P2 and therapeutical use)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 15 OF 25 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:360591 HCAPLUS
DOCUMENT NUMBER: 131:139718
TITLE: Stimulation of prolactin release by prolactin-releasing peptide in rats
AUTHOR(S): Matsumoto, Hirokazu; Noguchi, Jiro; Horikoshi, Yasuko; Kawamata, Yuji; Kitada, Chieko; Hinuma, Shuji; Onda, Haruo; Nishimura, Osamu; Fujino, Masahiko
CORPORATE SOURCE: Discovery Research Laboratories I, Pharmaceutical Discovery Division, Takeda Chemical Industries Ltd., Ibaraki, 300-4293, Japan
SOURCE: Biochem. Biophys. Res. Commun. (1999), 259(2), 321-324
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors have previously reported a hypothalamic peptide that shows specific prolactin (PRL)-releasing activity in vitro, named prolactin-releasing peptide (PrRP). However, its activity in vivo has not yet been shown. In this study, the authors examd. whether PrRP could induce specific PRL release in vivo using normal cycling female and male rats. I.v. injection of PrRP31 increased plasma PRL levels in rats in a dose-dependent manner. PrRP31 (50 nmol/kg i.v.) significantly ($P < 0.05$) stimulated plasma PRL levels within 25 min after injection in rats in proestrus, estrus, and metestrus. A higher dose of PrRP31 (500 nmol/kg i.v.) was necessary for a significant increase in plasma PRL levels in male rats. These results clearly indicate that female rats, esp. at proestrus, are more sensitive to PrRP-induced PRL secretion than male rats. The effect of PrRP on PRL release is affected considerably by the estrus cycle and sex, which suggests that PrRP sensitivity is controlled

by the endogenous hormonal milieu, such as estrogen levels. PrRP31 did not affect other pituitary hormone secretions. The results indicate that PrRP shows specific PRL-releasing activity in vivo as well as in vitro and suggest that it plays an important role in the regulation of PRL release under certain physiol. conditions. (c) 1999 Academic Press.

IT **215510-06-8**, Rat prolactin-releasing peptide 31
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(prolactin release stimulation by prolactin-releasing peptide in rat)

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 16 OF 25 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:353255 HCAPLUS
DOCUMENT NUMBER: 131:165905
TITLE: Synthesis of new peptides with prolactin-releasing activity by a combination of recombinant DNA technology and a cysteine-specific cyanylation reaction
AUTHOR(S): Nishimura, Osamu; Moriya, Takeo; Suenaga, Masato; Tanaka, Yoko; Itoh, Takashi; Koyama, Nobuyuki; Fujii, Ryo; Hinuma, Shuji; Kitada, Chieko; Fujino, Masahiko
CORPORATE SOURCE: Biotechnology Laboratories, Pharmaceutical Research Division, Takeda Chemical Industries, Ltd., Osaka, 532-8686, Japan
SOURCE: Pept. Sci. (1999), Volume Date 1998, 35th, 177-180
CODEN: PSCIFQ; ISSN: 1344-7661
PUBLISHER: Protein Research Foundation
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Prolactin-releasing peptide (PrRP) is a new peptide which was isolated in our research division. In the present study, bovine, rat, and human PrRPs, were synthesized by a combination of recombinant DNA technol. and a cysteine-specific cyanylation reaction. The purified peptides showed the same biol. activity as the chem. synthesized std. The peptides obtained here might be very useful for studies on their biol. significance and roles in vivo.

IT **209466-89-7P**, Prolactin-releasing peptide (cattle)
215510-06-8P, Prolactin-releasing peptide (rat)
215510-22-8P, Prolactin-releasing peptide (human)
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of new peptides with prolactin-releasing activity by combination of recombinant DNA technol. and cysteine-specific cyanation reaction)

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 17 OF 25 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:353216 HCAPLUS
DOCUMENT NUMBER: 131:139596
TITLE: Identification of prolactin-releasing peptide
AUTHOR(S): Fujii, Ryo; Habata, Yugo; Kawamata, Yuji; Hosoya, Masaki; Fukusumi, Shoji; Hinuma, Shuji; Matsumoto, Hirokazu; Kitada, Chieko; Kurokawa, Tsutomu; Nishimura, Osamu; Onda, Haruo; Fujino, Masahiko
CORPORATE SOURCE: Discovery Research Laboratories 1, Pharmaceutical Discovery Research Division, Takeda Chemical Industries, Ltd., Tsukuba, 300-4293, Japan
SOURCE: Pept. Sci. (1999), Volume Date 1998, 35th, 25-28

CODEN: PSCIFQ; ISSN: 1344-7661
PUBLISHER: Protein Research Foundation
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We isolated a novel orphan 7TMR cDNA, hGR3, from the human pituitary, and then searched for its endogenous ligand. We purified a ligand peptide for hGR3 from bovine hypothalamic tissue ext., and subsequently isolated bovine, rat, and human cDNAs encoding the peptide. As this peptide synthesized showed a specific prolactin (PRL)-releasing activity in rat anterior pituitary cells, we named it PRL-releasing peptide (PrRP). Our strategy employed here can be widely applied to identify ligands for many other orphan 7TMRs.
IT **215510-22-8**, Human PrRP-31 **235433-36-0**, Human PrRP-20
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BPR (Biological process); PRP (Properties); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(characterization, tissue distribution, and receptor interaction of human prolactin-releasing peptides)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 18 OF 25 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:151262 HCAPLUS
DOCUMENT NUMBER: 130:277038
TITLE: Gender-biased activity of the novel prolactin releasing peptides. Comparison with thyrotropin releasing hormone reveals only pharmacologic effects
AUTHOR(S): Samson, Willis K.; Resch, Zachary T.; Murphy, Tonya C.; Chang, Jaw-Kang
CORPORATE SOURCE: Department of Physiology, University of North Dakota School of Medicine, Grand Forks, ND, 58202, USA
SOURCE: Endocrine (1998), 9(3), 289-291
CODEN: EOCRE5; ISSN: 1355-008X
PUBLISHER: Humana Press Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The prolactin- (PRL) releasing activities of the newly described PRL-releasing peptides (PrRPs) were compared to that of TSH-releasing hormone (TRH) in dispersed, rat anterior pituitary cell cultures. A dose-related stimulation of PRL release by TRH was obsd. in cells harvested from both intact male and random cycle female pituitary donors. The min. ED of TRH ranged from 1 to 10 nM. Neither PrRP-20 nor PrRP-31 significantly altered PRL secretion in cells from male donors even at doses as high as 1 .mu.M. In cells harvested from females, only the highest doses of PrRP-20 and PrRP-31 tested (0.1 and 1.0 .mu.M) significantly stimulated PRL secretion. The PRL-releasing action of TRH was obsd. already at 15 min of incubation, whereas those of PrRP-20 and PrRP-31 appeared only after 1 and 2 h of incubation, and the magnitude of PRL release in the presence of 1 .mu.M PrRPs was significantly less than that of a similar dose of TRH. These data do not suggest a physiol. relevant role for the PrRPs in the neuroendocrine regulation of PRL secretion in intact male and nonlactating, random-cycle female rats.
IT **215510-22-8**, Human PrRP-31 **2229BB-10-5**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(gender-biased activity of prolactin releasing peptides and comparison with TRH in male and female rat anterior pituitary cell cultures)
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 19 OF 25 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:32028 HCAPLUS
DOCUMENT NUMBER: 130:94530
TITLE: Method of producing a 19p2 ligand/prolactin-releasing peptide by cleavage of a recombinant fusion protein
INVENTOR(S): Suenaga, Masato; Moriya, Takeo; Tanaka, Yoko; Nishimura, Osamu
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: Eur. Pat. Appl., 56 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 887417	A2	19981230	EP 1998-111725	19980625
EP 887417	A3	19990113		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CA 2242086	AA	19981227	CA 1998-2242086	19980626
JP 11071396	A2	19990316	JP 1998-180555	19980626
US 6103882	A	20000815	US 1998-105678	19980626
US 6258561	B1	20010710	US 1999-421208	19991020

PRIORITY APPLN. INFO.: JP 1997-172118 A 19970627
JP 1997-17218 A 19970627
US 1998-105678 A3 19980626

AB The method of the present invention is suitable for the com. high-level prodn. of a protein or peptide which can be used as a prophylactic and therapeutic drug. Thus, plasmid pTB960-10, contg. a chimeric gene encoding prolactin-releasing peptide fused to the N-terminus of cysteinyl-basic fibroblast growth factor, was prepd. Escherichia coli transformed with this plasmid was used to prep. the peptide. The peptide was released from the fusion protein by a process comprising cyanylation followed by hydrolysis or ammonolysis.

IT **191919-77-4P 192588-09-3P 192588-12-8P**
209466-89-7P 215510-06-8P 215510-22-8P
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method of producing 19p2 ligand/prolactin-releasing peptide by cleavage of recombinant fusion protein)

L2 ANSWER 20 OF 25 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:27860 HCAPLUS
DOCUMENT NUMBER: 130:91922
TITLE: sequence and therapeutic applications for mouse and human and bovine and rat prolactin secretion modulator peptides as ligands for G-protein coupled receptors
INVENTOR(S): Hinuma, Shuji; Kawamata, Yuji; Fujii, Ryo; Matsumoto, Hirokazu
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 242 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9858962	A1	19981230	WO 1998-JP2765	19980622
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GW, HU, ID, IL, IS, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9880373	A1	19990104	AU 1998-80373	19980622
JP 11071300	A2	19990316	JP 1998-175007	19980622
EP 1001989	A1	20000524	EP 1998-928607	19980622
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: JP 1997-165437 19970623
WO 1998-JP2765 19980622

AB The present invention relates to a ligand polypeptide prolactin secretion modulating activity, and has a function of modulating placental function. The ligand polypeptide can be used as a prolactin secretion-stimulating agent for the prevention and treatment of certain diseases assocd. with prolactin secretion, such as hypoovarianism, gonecyst cacogenesis, menopausal syndrome, and euthyroid hypometabolism. Bovine and human and mouse and rat ligand sequences are presented. In addn., the ligand polypeptide of the invention can be used with advantage as an aphrodisiac. The ligand polypeptide of the invention can be used with advantage as a prolactin secretion inhibitory agent in the prevention and treatment of certain diseases assocd. with prolactin secretion, such as pituitary adenomatosis, brain tumor, emmeniopathy, autoimmune disease, prolactinoma, infertility, impotence, amenorrhea, galactorrhea, acromegaly, Chiari-Frommel syndrome, Argonz-del Castilo syndrome, Forbes-Albright syndrome, lymphoma, Sheehan syndrome or dyszoospermia. In addn., the ligand polypeptide of the present invention is used as an agent for treating or preventing choriocarcinoma, hydatid mole, irruption mole, abortion, un-thrifty fetus, abnormal saccharometabolism, abnormal lipid metab. or oxytocia. A method is described for activating the release of arachidonic acid metabolites using these peptides. Therapeutic administration of these peptides resulted in decreased levels of growth hormone and hypertension and hyperkinesia.

IT **191919-77-4 191919-78-5**
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bovine amino acid sequence of G protein-coupled receptor ligand fragment promoting/inhibiting prolactin secretion; sequence and therapeutic applications for prolactin secretion modulator peptides)

IT **192588-12-B**
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human amino acid sequence of G protein-coupled receptor ligand fragment promoting/inhibiting prolactin secretion; sequence and therapeutic applications for prolactin secretion modulator peptides)

IT **191919-81-0 192588-09-3**
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(rat amino acid sequence of G protein-coupled receptor ligand fragment promoting/inhibiting prolact n secretion; sequence and therapeutic applications for prolactin secretion modulator peptides)

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 21 OF 25 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:728552 HCAPLUS
DOCUMENT NUMBER: 130:836
TITLE: An endogenous pituitary-derived protein ligand for a G protein-coupled receptor, a cDNA encoding it, and their therapeutic uses
INVENTOR(S): Hinuma, Shuji; Fukusumi, Shoji
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 206 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9849295	A1	19981105	WO 1998-JP1923	19980427
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GW, HU, ID, IL, IS, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9870817	A1	19981124	AU 1998-70817	19980427
JP 11009286	A2	19990119	JP 1998-117189	19980427
EP 981616	A1	20000301	EP 1998-917693	19980427
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: JP 1997-109974 19970428
WO 1998-JP1923 19980427

AB A ligand for an orphan G protein-coupled receptor of the mouse pituitary gland is identified and a cDNA encoding it is cloned. The receptor and its ligand may be targets for the development of therapeutic agents for a no. of mental disorders and diseases of the pancreas. The receptor cDNA was cloned by PCR using primers derived from conserved sequences of G protein-coupled receptors. Individual PCR products were cloned and sequenced and the sequences screened for extended homol. to other G protein-coupled receptors. The cDNA was expressed in CHO cells using the pAKKO-111H vector system. Cells expressing the receptor gene were then used to assay for factors stimulating arachidonic acid metabolite release in rat brain exts. An activity was detected after fractionation and an activity showing the same properties was found in cattle brain exts. and purified to homogeneity. Three peaks of activity were found and characterized. CDNAs were cloned by RT-PCR. Biol. activity of the peptides was confirmed using chem. synthesized peptides.

IT **209466-89-7P 215510-10-4P**
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(amino acid sequence, synthesis and biol. activity of; endogenous pituitary-derived protein ligand for G protein-coupled receptor, cDNA encoding it, and their therapeutic uses)

IT **215796-45-5DP**, conjugate with PMBHA resin
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP

(Preparation)
(amino acid sequence, synthesis of; endogenous pituitary-derived protein ligand for G protein-coupled receptor, cDNA encoding it, and their therapeutic uses)
IT **191919-77-4 192588-09-3 215662-80-9**
215662-83-2
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; endogenous pituitary-derived protein ligand for G protein-coupled receptor, cDNA encoding it, and their therapeutic uses)
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 22 OF 25 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:634917 HCAPLUS
DOCUMENT NUMBER: 129:340313
TITLE: Synthesis of new peptides with prolactin-releasing activity by a combination of recombinant DNA technology and a cysteine-specific cyanylation reaction
AUTHOR(S): Nishimura, Osamu; Moriya, Takeo; Suenaga, Masato; Tanaka, Yoko; Itoh, Takashi; Koyama, Nobuyuki; Fujii, Ryo; Hinuma, Shuji; Kitada, Chieko; Fujino, Masahiko
CORPORATE SOURCE: Biotechnology Laboratories, Pharmaceutical Research Division, Takeda Chemical Industries, Ltd., Osaka, 532-8686, Japan
SOURCE: Chem. Pharm. Bull. (1998), 46(9), 1490-1492
CODEN: CPBTAL; ISSN: 0009-2363
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A newly isolated peptide from bovine hypothalamus with prolactin-releasing activity (prolactin-releasing peptide; PrRP) was synthesized by a combination of recombinant DNA technol. and a cysteine-specific cyanylation reaction, together with rat and human homologs. The peptides were expressed in the form of fusion proteins with basic fibroblast growth factor mutein, which were purified by heparin-affinity chromatog. The fusion proteins were cleaved at the cysteine residues of the junction site by cyanylation, followed by treatment with ammonia for C-terminal amidation. Purifn. of the resulting crude peptides was performed using chromatog. on a gel-filtration column, a cation-exchange column, and a reversed-phase column. As an example, about 90 mg of bovine PrRP (bPrRP) was obtained from 20 l of culture broth. The purified bPrRP showed full biol. activities in binding to its receptor expressed on CHO cells and releasing arachidonic acid metabolite from the same cells, while the C-terminal acid form of bPrRP had little of these activities. These results indicate that the C-terminal amide structure is very important for expressing biol. activity. The peptides obtained here might be very useful for studies on their biol. significance and roles in vivo.
IT **209466-89-7P**
RL: BPN (Biosynthetic preparation); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(bovine prolactin-releasing peptide; prolactin-releasing peptide syntheses by combination of recombinant DNA technol. and cysteine-specific cyanylation reaction)
IT **215510-22-8P**
RL: BPN (Biosynthetic preparation); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(human prolactin-releasing peptide; prolactin-releasing peptide

syntheses by combination of recombinant DNA technol. and cysteine-specific cyanylation reaction)

IT **215510-06-8P**
RL: BPN (Biosynthetic preparation); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(rat prolactin-releasing peptide; prolactin-releasing peptide syntheses by combination of recombinant DNA technol. and cysteine-specific cyanylation reaction)

L2 ANSWER 23 OF 25 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:486145 HCAPLUS
DOCUMENT NUMBER: 129:211873
TITLE: A prolactin-releasing peptide in the brain. [Erratum to document cited in CA129:76746]
AUTHOR(S): Hinuma, Shuji; Habata, Yugo; Fujii, Ryo; Kawamata, Yuji; Hosoya, Masaki; Fukusumi, Shoji; Kitada, Chieko; Masuo, Yoshinori; Asano, Tsuneo; Matsumoto, Hirokazu; Sekiguchi, Masahiro; Kurokawa, Tsutomu; Nishimura, Osamu; Onda, Haruo; Fujino, Masahiko
CORPORATE SOURCE: Discovery Res. Laboratories I., Pharmaceutical Discovery Res. Division, Takeda Chem. Industries Ltd., Tsukuba, 300-4293, Japan
SOURCE: Nature (London) (1998), 394(6690), 302
CODEN: NATUAS; ISSN: 0028-0836
PUBLISHER: Macmillan Magazines
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The prolactin-releasing peptide cDNA sequence data were submitted to the DDBJ/EMBL/GenBank databases. The accession nos. are as follows: AB015417, Bos taurus mRNA for preproprolactin-releasing peptide; AB015418, Rattus norvegicus mRNA for preproprolactin-releasing peptide; and AB015419, Homo sapiens mRNA for preproprolactin-releasing peptide.
IT **192526-83-3 192526-94-6 192527-01-8**
RL: PRP (Properties)
(amino acid sequence; prolactin-releasing peptides (protein) (Erratum))
IT **209466-89-7P 209466-90-0P**
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation)
(prolactin-releasing peptides (protein) (Erratum))

L2 ANSWER 24 OF 25 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:338679 HCAPLUS
DOCUMENT NUMBER: 129:76746
TITLE: A prolactin-releasing peptide in the brain
AUTHOR(S): Hinuma, Shuji; Habata, Yugo; Fujii, Ryo; Kawamata, Yuji; Hosoya, Masaki; Fukusumi, Shoji; Kitada, Chieko; Masuo, Yoshinori; Asano, Tsuneo; Matsumoto, Hirokazu; Sekiguchi, Masahiro; Kurokawa, Tsutomu; Nishimura, Osamu; Onda, Haruo; Fujino, Masahiko
CORPORATE SOURCE: Discovery Res. Laboratories I, Pharmaceutical Discovery Res. Division, Takeda Chem. Industries Ltd., Tsukuba, Ibaraki, 300-4293, Japan
SOURCE: Nature (London) (1998), 393(6682), 272-276
CODEN: NATUAS; ISSN: 0028-0836
PUBLISHER: Macmillan Magazines
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Hypothalamic peptide hormones regulate the secretion of most of the

anterior pituitary hormones, i.e., growth hormone, FSH, LH, TSH and ACTH. These peptides do not regulate the secretion of prolactin, at least in a specific manner, however. The peptides act through specific receptors, which are referred to as seven-transmembrane-domain receptors or G-protein-coupled receptors. Although prolactin is important in pregnancy and lactation in mammals, and is involved in the development of the mammary glands and the promotion of milk synthesis, a specific prolactin-releasing hormone has remained unknown. Here the authors identify a potent candidate for such a hormone. The authors first proposed that there may still be unknown peptide hormone factors that control pituitary function through seven-transmembrane-domain receptors. The authors isolated the cDNA encoding an 'orphan' receptor (i.e., one for which the ligand is unknown). This receptor, hGR3, is specifically expressed in the human pituitary. The authors then searched for the hGR3 ligand in the hypothalamus and identified a new peptide, which shares no sequence similarity with known peptides and proteins, as an endogenous ligand. The authors show that this ligand is a potent prolactin-releasing factor for rat anterior pituitary cells; the authors have therefore named this peptide prolactin-releasing peptide.

IT **209466-B9-7P 209466-90-0P**
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation)
(prolactin-releasing peptides (protein))

L2 ANSWER 25 OF 25 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:476315 HCAPLUS
DOCUMENT NUMBER: 127:118270
TITLE: Ligand polypeptides for the G-protein-coupled receptor proteins from human pituitary and mouse pancreas
INVENTOR(S): Hinuma, Shuji; Habata, Yugo; Kawamata, Yuji; Hosoya, Masaki; Fujii, Ryo; Fukusumi, Shoji; Kitada, Chieko
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan; Hinuma, Shuji; Habata, Yugo; Kawamata, Yuji; Hosoya, Masaki; Fujii, Ryo; Fukusumi, Shoji; Kitada, Chieko
SOURCE: PCT Int. Appl., 258 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9724436	A2	19970710	WO 1996-JP3821	19961226
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2239299	AA	19970710	CA 1996-2239299	19961226
AU 9712084	A1	19970728	AU 1997-12084	19961226
JP 10146192	A2	19980602	JP 1996-348328	19961226
EP 870020	A2	19981014	EP 1996-943306	19961226
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1207126	A	19990203	CN 1996-199382	19961226

US 6228984 B1 20010508 US 1997-776971 19970207
PRIORITY APPLN. INFO.: JP 1995-343371 A 19951228
JP 1996-59419 A 19960315
JP 1996-211805 A 19960812
JP 1996-246573 A 19960918
WO 1996-JP3821 W 19961226
OTHER SOURCE(S): MARPAT 127:118270

AB Ligand polypeptides are provided for human pituitary- and mouse pancreas-derived G protein-coupled receptor proteins. Thus, human pituitary or mouse pancreatic receptor protein cDNAs were identified and cloned into animal cells to allow screening for binding ligand polypeptides. Ligand polypeptide cDNAs were isolated and sequenced from bovine, rat, and human. The 3 G-protein-coupled receptor ligands comprise 98, 83, and 87 amino acid residues, resp., and contain the partial sequence TPDINPAWY-X1-X2-RGIRPVGRF-X3, where X1 = Ala or Thr, X2 = Gly or Ser, and X3 = H, Gly, or Gly-Arg. The ligand polypeptide or the DNA which encodes for the ligand polypeptide can be used for (1) development of medicines such as pituitary function modulators, central nervous system function modulators, and pancreatic function modulators, and (2) development of receptor binding assay systems using the expression of recombinant receptor proteins and screening of pharmaceutical candidate compds. In particular, by the receptor binding assay systems utilizing the expression of recombinant G protein-coupled receptor proteins in accordance with the invention, agonists and antagonists of G protein-coupled receptors which are specific to human and other warm-blooded animals can be screened and the agonists or antagonists obtained can be used as therapeutic and prophylactic agents for various diseases.

IT **192526-83-3P 192526-94-6P 192527-01-8P**
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; ligand polypeptides for the G-protein-coupled receptor proteins from human pituitary and mouse pancreas)

IT **191919-77-4P 191919-78-5P 191919-79-6P**
191919-80-9P 192588-11-7P 192588-15-1P
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(bovine ligand fragment; ligand polypeptides for the G-protein-coupled receptor proteins from human pituitary and mouse pancreas)

IT **191919-84-3P 191919-85-4P 191919-86-5P**
192588-12-8P 192588-13-9P 192588-16-2P
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(human ligand fragment; ligand polypeptides for the G-protein-coupled receptor proteins from human pituitary and mouse pancreas)

IT **191919-81-0P 191919-82-1P 191919-83-2P**
192588-09-3P 192588-10-6P 192588-14-0P
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(rat ligand fragment; ligand polypeptides for the G-protein-coupled receptor proteins from human pituitary and mouse pancreas)

=>
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=> fil reg
FILE 'REGISTRY' ENTERED AT 12:02:33 ON 01 APR 2002
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DICTIONARY FILE UPDATES: 31 MAR 2002 HIGHEST RN 403640-18-6

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

The P indicator for Preparations was not generated for all of the CAS Registry Numbers that were added to the H/Z/CA/CAplus files between 12/27/01 and 1/23/02. Use of the P indicator in online and SOI searches during this period, either directly appended to a CAS Registry Number or by qualifying an L-number with /P, may have yielded incomplete results. As of 1/23/02, the situation has been resolved. Also, note that searches conducted using the PREP role indicator were not affected.

Customers running searches and/or SDIs in the H/Z/CA/CAplus files incorporating CAS Registry Numbers with the P indicator between 12/27/01 and 1/23/02, are encouraged to re-run these strategies. Contact the CAS Help Oesk at 1-800-848-6533 in North America or 1-614-447-3698, worldwide, or send an e-mail to help@cas.org for further assistance or to receive a credit for any duplicate searches.

=>
=>
=> d .seq l1 1-32

L1 ANSWER 1 OF 32 REGISTRY COPYRIGHT 2002 ACS
RN 309255-64-9 REGISTRY
CN 164: PN: WO0069900 SEQID: 169 unclaimed protein (9CI) (CA INDEX NAME)
SQL 31

SEQ 1 SRAHQHSMEI RTPOINPAWY ASRGIRPVGR F
========= ========== =
HITS AT: 12-31

REFERENCE 1: 134:21425

L1 ANSWER 2 OF 32 REGISTRY COPYRIGHT 2002 ACS
RN 235433-36-0 REGISTRY
CN L-Phenylalaninamide, L-threonyl-L-prolyl-L-.alpha.-aspartyl-L-isoleucyl-L-asparaginyl-L-prolyl-L-alanyl-L-tryptophyl-L-tyrosyl-L-alanyl-L-seryl-L-arginylglycyl-L-isoleucyl-L-arginyl-L-prolyl-L-valylglycyl-L-arginyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 12-31-Human prolactin-releasing peptide
CN Human PrRP-20
CN Prolactin-releasing peptide-20 (human)
NTE modified
---

type	------ location ------		description
terminal mod.	Phe-20	-	C-terminal amide

SQL 20

SEQ 1 TPDINPAWYA SRGIRPVGRF
========== ==========

HITS AT: 1-20

REFERENCE 1: 134:13518

REFERENCE 2: 132:59425

REFERENCE 3: 131:139596

L1 ANSWER 3 OF 32 REGISTRY COPYRIGHT 2002 ACS
RN 222988-10-5 REGISTRY
CN L-Phenylalaninamide, L-threonyl-L-prolyl-L-.alpha.-aspartyl-L-isoleucyl-L-asparaginyl-L-prolyl-L-alanyl-L-tryptophyl-L-tyrosyl-L-threonylglycyl-L-arginylglycyl-L-isoleucyl-L-arginyl-L-prolyl-L-valylglycyl-L-arginyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Rat prolactin-releasing peptide 12-31
CN Rat prolactin-releasing peptide-20
NTE modified

type	------ location ------		description
terminal mod.	Phe-20	-	C-terminal amide

SQL 20

SEQ 1 TPDINPAWYT GRGIRPVGRF
========== ==========

HITS AT: 1-20

REFERENCE 1: 134:13518

REFERENCE 2: 133:53944

REFERENCE 3: 132:274519

REFERENCE 4: 130:277038

L1 ANSWER 4 OF 32 REGISTRY COPYRIGHT 2002 ACS
RN 215796-45-5 REGISTRY
CN L-Phenylalanine, O-(phenylmethyl)-L-seryl-N5-[imino[[(4-methylphenyl)sulfonyl]amino]methyl]-L-ornithyl-L-alanyl-1-[(phenylmethoxy)methyl]-L-histidyl-L-glutaminyl-1-[(phenylmethoxy)methyl]-L-histidyl-O-(phenylmethyl)-L-seryl-L-methionyl-L-.alpha.-glutamyl-L-isoleucyl-N5-[imino[[(4-methylphenyl)sulfonyl]amino]methyl]-L-ornithyl-O-(phenylmethyl)-L-threonyl-L-prolyl-L-.alpha.-aspartyl-L-isoleucyl-L-asparaginyl-L-prolyl-L-alanyl-1-formyl-L-tryptophyl-O-[[(2-bromophenyl)methoxy]carbonyl]-L-tyrosyl-L-alanylglycyl-N5-[imino[[(4-methylphenyl)sulfonyl]amino]methyl]-L-ornithylglycyl-L-isoleucyl-N5-[imino[[(4-methylphenyl)sulfonyl]amino]methyl]-L-ornithyl-L-prolyl-L-valylglycyl-N5-[imino[[(4-methylphenyl)sulfonyl]amino]methyl]-L-ornithyl-, 9,14-dicyclohexyl ester (9CI) (CA INDEX NAME)

```
NTE  modified (modifications unspecified)
SQL  31

SEQ      1 SRAHQHSMEI RTPDINPAWY AGRGIRPVGR F
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HITS AT:   1-31

REFERENCE   1:  130:836

L1   ANSWER 5 OF 32  REGISTRY  COPYRIGHT 2002 ACS
RN   215662-83-2  REGISTRY
CN   Protein (cattle G protein-coupled receptor ligand precursor) (9CI)  (CA
     INDEX NAME)
OTHER NAMES:
CN   15: PN: WO0135984 SEQID: 15 unclaimed protein
SQL  98

SEQ      1 MKAVGAWLLC LLLLGLALQG AASRAHQHSM EIRTPDINPA WYAGRGIRPV
                                   ======== ========== ==========
        51 GRFGRRRAAL GDGPRPGPRR VPACFRLEGG AEPSRALPGR LTAQLVQE
           ===
HITS AT:   23-53

REFERENCE   1:  135:14693

REFERENCE   2:  130:836

L1   ANSWER 6 OF 32  REGISTRY  COPYRIGHT 2002 ACS
RN   215662-80-9  REGISTRY
CN   Protein (mouse clone pBOV3 G protein-coupled receptor ligand precursor)
     (9CI)  (CA INDEX NAME)
SQL  82

SEQ      1 APRTWLLCLL LLGLVLPGAS SRAHQHSMET RTPDINPAWY TGRGIRPVGR
                                 ========== ========== ==========
        51 FGRRRAALRD VTGPGLRCRL SCFPLDGSAK FS
           =
HITS AT:   21-51

REFERENCE   1:  130:836

L1   ANSWER 7 OF 32  REGISTRY  COPYRIGHT 2002 ACS
RN   215510-22-8  REGISTRY
CN   L-Phenylalaninamide, L-seryl-L-arginyl-L-threonyl-L-histidyl-L-arginyl-L-
     histidyl-L-seryl-L-methionyl-L-.alpha.-glutamyl-L-isoleucyl-L-arginyl-L-
     threonyl-L-prolyl-L-.alpha.-aspartyl-L-isoleucyl-L-asparaginyl-L-prolyl-L-
     alanyl-L-tryptophyl-L-tyrosyl-L-alanyl-L-seryl-L-arginylglycyl-L-isoleucyl-
     L-arginyl-L-prolyl-L-valylglycyl-L-arginyl- (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   2: PN: WO9960112 SEQID: 2 claimed protein
CN   Human prolactin-releasing peptide
CN   Human PrRP-31
CN   Prolactin-releasing peptide (human)
CN   Prolactin-releasing peptide-31 (human)
NTE  modified
-------------------------------------------------------------------
 type            ------ location ------         description
-------------------------------------------------------------------
terminal mod.    Phe-31          -         C-terminal amide
```

```
SQL  31

SEQ      1 SRTHRHSMEI RTPDINPAWY ASRGIRPVGR F
           ========== ========== ========== =
HITS AT:   1-31

REFERENCE   1:  134:13518

REFERENCE   2:  132:59425

REFERENCE   3:  132:11632

REFERENCE   4:  131:165905

REFERENCE   5:  131:139596

REFERENCE   6:  130:277038

REFERENCE   7:  130:94530

REFERENCE   8:  129:340313

L1   ANSWER 8 OF 32  REGISTRY  COPYRIGHT 2002 ACS
RN   215510-10-4  REGISTRY
CN   L-Phenylalaninamide, L-seryl-L-arginyl-L-alanyl-L-histidyl-L-glutaminyl-L-
     histidyl-L-seryl-(2R)-2-amino-4-(methylsulfinyl)butanoyl-L-.alpha.-
     glutamyl-L-isoleucyl-L-arginyl-L-threonyl-L-prolyl-L-.alpha.-aspartyl-L-
     isoleucyl-L-asparaginyl-L-prolyl-L-alanyl-L-tryptophyl-L-tyrosyl-L-
     alanylglycyl-L-arginylglycyl-L-isoleucyl-L-arginyl-L-prolyl-L-valylglycyl-
     L-arginyl- (9CI)  (CA INDEX NAME)
NTE  modified (modifications unspecified)
SQL  31

SEQ      1 SRAHQHSMEI RTPDINPAWY AGRGIRPVGR F
           ========== ========== ========== =
HITS AT:   1-31

REFERENCE   1:  130:836

L1   ANSWER 9 OF 32  REGISTRY  COPYRIGHT 2002 ACS
RN   215510-06-8  REGISTRY
CN   L-Phenylalaninamide, L-seryl-L-arginyl-L-alanyl-L-histidyl-L-glutaminyl-L-
     histidyl-L-seryl-L-methionyl-L-.alpha.-glutamyl-L-threonyl-L-arginyl-L-
     threonyl-L-prolyl-L-.alpha.-aspartyl-L-isoleucyl-L-asparaginyl-L-prolyl-L-
     alanyl-L-tryptophyl-L-tyrosyl-L-threonylglycyl-L-arginylglycyl-L-isoleucyl-
     L-arginyl-L-prolyl-L-valylglycyl-L-arginyl- (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   1: PN: WO0017641 PAGE: 12 claimed protein
CN   Prolactin-releasing peptide (rat)
CN   Rat prolactin-releasing peptide 31
NTE  modified
-------------------------------------------------------------------------
 type            ------ location ------         description
-------------------------------------------------------------------------
terminal mod.    Phe-31          -         C-terminal amide
-------------------------------------------------------------------------
SQL  31
```

```
SEQ      1 SRAHQHSMET RTPDINPAWY TGRGIRPVGR F
           ========== ========== ========== =
HITS AT:   1-31

REFERENCE   1:  135:175761

REFERENCE   2:  134:66407

REFERENCE   3:  134:13518

REFERENCE   4:  133:53944

REFERENCE   5:  132:274519

REFERENCE   6:  132:260688

REFERENCE   7:  131:165905

REFERENCE   8:  131:139718

REFERENCE   9:  130:94530

REFERENCE  10:  129:340313

L1   ANSWER 10 OF 32  REGISTRY  COPYRIGHT 2002 ACS
RN   209466-90-0  REGISTRY
CN   L-Phenylalaninamide, L-threonyl-L-prolyl-L-.alpha.-aspartyl-L-isoleucyl-L-
     asparaginyl-L-prolyl-L-alanyl-L-tryptophyl-L-tyrosyl-L-alanylglycyl-L-
     arginylglycyl-L-isoleucyl-L-arginyl-L-prolyl-L-valylglycyl-L-arginyl-
     (9CI)  (CA INDEX NAME)
NTE  modified
-------------------------------------------------------------------------
 type            ------ location ------         description
-------------------------------------------------------------------------
terminal mod.    Phe-20          -         C-terminal amide
-------------------------------------------------------------------------
SQL  20

SEQ      1 TPDINPAWYA GRGIRPVGRF
           ========== ==========
HITS AT:   1-20

REFERENCE   1:  134:142305

REFERENCE   2:  129:211873

REFERENCE   3:  129:76746

L1   ANSWER 11 OF 32  REGISTRY  COPYRIGHT 2002 ACS
RN   209466-89-7  REGISTRY
CN   L-Phenylalaninamide, L-seryl-L-arginyl-L-alanyl-L-histidyl-L-glutaminyl-L-
     histidyl-L-seryl-L-methionyl-L-.alpha.-glutamyl-L-isoleucyl-L-arginyl-L-
     threonyl-L-prolyl-L-.alpha.-aspartyl-L-isoleucyl-L-asparaginyl-L-prolyl-L-
     alanyl-L-tryptophyl-L-tyrosyl-L-alanylglycyl-L-arginylglycyl-L-isoleucyl-L-
     arginyl-L-prolyl-L-valylglycyl-L-arginyl- (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   Prolactin-releasing peptide (cattle)
CN   Prolactin-releasing peptide 31
CN   Prolactin-releasing peptide PrRP31
```

```
NTE  modified
----------------------------------------------------------------------
 type            ------ location ------         description
----------------------------------------------------------------------
terminal mod.    Phe-31          -         C-terminal amide
----------------------------------------------------------------------
SQL  31

SEQ      1 SRAHQHSMEI RTPDINPAWY AGRGIRPVGR F
           ========== ========== ========== =
HITS AT:   1-31

REFERENCE   1:  135:327590

REFERENCE   2:  131:165905

REFERENCE   3:  130:94530

REFERENCE   4:  130:836

REFERENCE   5:  129:340313

REFERENCE   6:  129:211873

REFERENCE   7:  129:76746

L1   ANSWER 12 OF 32  REGISTRY  COPYRIGHT 2002 ACS
RN   192588-16-2  REGISTRY
CN   L-Arginine, L-seryl-L-arginyl-L-threonyl-L-histidyl-L-arginyl-L-histidyl-L-
     seryl-L-methionyl-L-.alpha.-glutamyl-L-isoleucyl-L-arginyl-L-threonyl-L-
     prolyl-L-.alpha.-aspartyl-L-isoleucyl-L-asparaginyl-L-prolyl-L-alanyl-L-
     tryptophyl-L-tyrosyl-L-alanyl-L-seryl-L-arginylglycyl-L-isoleucyl-L-
     arginyl-L-prolyl-L-valylglycyl-L-arginyl-L-phenylalanylglycyl- (9CI)  (CA
     INDEX NAME)
OTHER NAMES:
CN   33: PN: WO0135984 SEQID: 34 unclaimed protein
SQL  33

SEQ      1 SRTHRHSMEI RTPDINPAWY ASRGIRPVGR FGR
           ========== ========== ========== =
HITS AT:   1-31

REFERENCE   1:  135:14693

REFERENCE   2:  127:118270

L1   ANSWER 13 OF 32  REGISTRY  COPYRIGHT 2002 ACS
RN   192588-15-1  REGISTRY
CN   L-Arginine, L-seryl-L-arginyl-L-alanyl-L-histidyl-L-glutaminyl-L-histidyl-
     L-seryl-L-methionyl-L-.alpha.-glutamyl-L-isoleucyl-L-arginyl-L-threonyl-L-
     prolyl-L-.alpha.-aspartyl-L-isoleucyl-L-asparaginyl-L-prolyl-L-alanyl-L-
     tryptophyl-L-tyrosyl-L-alanylglycyl-L-arginylglycyl-L-isoleucyl-L-arginyl-
     L-prolyl-L-valylglycyl-L-arginyl-L-phenylalanylglycyl- (9CI)  (CA INDEX
     NAME)
OTHER NAMES:
CN   5: PN: WO0135984 SEQID: 5 unclaimed protein
CN   7: PN: WO9960112 SEQID: 8 claimed protein
SQL  33
```

```
SEQ      1 SRAHQHSMEI RTPDINPAWY AGRGIRPVGR FGR
           ========== ========== ========== =
HITS AT:   1-31

REFERENCE   1:  135:14693

REFERENCE   2:  132:11632

REFERENCE   3:  127:118270

L1   ANSWER 14 OF 32  REGISTRY  COPYRIGHT 2002 ACS
RN   192588-14-0  REGISTRY
CN   L-Arginine, L-seryl-L-arginyl-L-alanyl-L-histidyl-L-glutaminyl-L-histidyl-
     L-seryl-L-methionyl-L-.alpha.-glutamyl-L-threonyl-L-arginyl-L-threonyl-L-
     prolyl-L-.alpha.-aspartyl-L-isoleucyl-L-asparaginyl-L-prolyl-L-alanyl-L-
     tryptophyl-L-tyrosyl-L-threonylglycyl-L-arginylglycyl-L-isoleucyl-L-
     arginyl-L-prolyl-L-valylglycyl-L-arginyl-L-phenylalanylglycyl- (9CI)  (CA
     INDEX NAME)
OTHER NAMES:
CN   1: PN: WO0135984 SEQID: 20 unclaimed protein
SQL  33

SEQ      1 SRAHQHSMET RTPDINPAWY TGRGIRPVGR FGR
           ========== ========== ========== =
HITS AT:   1-31

REFERENCE   1:  135:14693

REFERENCE   2:  127:118270

L1   ANSWER 15 OF 32  REGISTRY  COPYRIGHT 2002 ACS
RN   192588-13-9  REGISTRY
CN   Glycine, L-seryl-L-arginyl-L-threonyl-L-histidyl-L-arginyl-L-histidyl-L-
     seryl-L-methionyl-L-.alpha.-glutamyl-L-isoleucyl-L-arginyl-L-threonyl-L-
     prolyl-L-.alpha.-aspartyl-L-isoleucyl-L-asparaginyl-L-prolyl-L-alanyl-L-
     tryptophyl-L-tyrosyl-L-alanyl-L-seryl-L-arginylglycyl-L-isoleucyl-L-
     arginyl-L-prolyl-L-valylglycyl-L-arginyl-L-phenylalanyl- (9CI)  (CA INDEX
     NAME)
OTHER NAMES:
CN   32: PN: WO0135984 SEQID: 33 unclaimed protein
SQL  32

SEQ      1 SRTHRHSMEI RTPDINPAWY ASRGIRPVGR FG
           ========== ========== ========== =
HITS AT:   1-31

REFERENCE   1:  135:14693

REFERENCE   2:  127:118270

L1   ANSWER 16 OF 32  REGISTRY  COPYRIGHT 2002 ACS
RN   192588-12-8  REGISTRY
CN   L-Phenylalanine, L-seryl-L-arginyl-L-threonyl-L-histidyl-L-arginyl-L-
     histidyl-L-seryl-L-methionyl-L-.alpha.-glutamyl-L-isoleucyl-L-arginyl-L-
     threonyl-L-prolyl-L-.alpha.-aspartyl-L-isoleucyl-L-asparaginyl-L-prolyl-L-
     alanyl-L-tryptophyl-L-tyrosyl-L-alanyl-L-seryl-L-arginylglycyl-L-isoleucyl-
     L-arginyl-L-prolyl-L-valylglycyl-L-arginyl- (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   130: PN: WO0069900 SEQID: 165 unclaimed protein
```

```
CN   31: PN: WO0135984 SEQID: 32 claimed protein
SQL  31

SEQ      1 SRTHRHSMEI RTPDINPAWY ASRGIRPVGR F
           ========== ========== ========== =
HITS AT:   1-31

REFERENCE   1:  135:14693

REFERENCE   2:  134:21425

REFERENCE   3:  133:79323

REFERENCE   4:  130:94530

REFERENCE   5:  130:91922

REFERENCE   6:  127:118270

L1   ANSWER 17 OF 32  REGISTRY  COPYRIGHT 2002 ACS
RN   192588-11-7  REGISTRY
CN   Glycine, L-seryl-L-arginyl-L-alanyl-L-histidyl-L-glutaminyl-L-histidyl-L-
     seryl-L-methionyl-L-.alpha.-glutamyl-L-isoleucyl-L-arginyl-L-threonyl-L-
     prolyl-L-.alpha.-aspartyl-L-isoleucyl-L-asparaginyl-L-prolyl-L-alanyl-L-
     tryptophyl-L-tyrosyl-L-alanylglycyl-L-arginylglycyl-L-isoleucyl-L-arginyl-
     L-prolyl-L-valylglycyl-L-arginyl-L-phenylalanyl- (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   4: PN: WO0135984 SEQID: 4 unclaimed protein
SQL  32

SEQ      1 SRAHQHSMEI RTPDINPAWY AGRGIRPVGR FG
           ========== ========== ========== =
HITS AT:   1-31

REFERENCE   1:  135:14693

REFERENCE   2:  127:118270

L1   ANSWER 18 OF 32  REGISTRY  COPYRIGHT 2002 ACS
RN   192588-10-6  REGISTRY
CN   Glycine, L-seryl-L-arginyl-L-alanyl-L-histidyl-L-glutaminyl-L-histidyl-L-
     seryl-L-methionyl-L-.alpha.-glutamyl-L-threonyl-L-arginyl-L-threonyl-L-
     prolyl-L-.alpha.-aspartyl-L-isoleucyl-L-asparaginyl-L-prolyl-L-alanyl-L-
     tryptophyl-L-tyrosyl-L-threonylglycyl-L-arginylglycyl-L-isoleucyl-L-
     arginyl-L-prolyl-L-valylglycyl-L-arginyl-L-phenylalanyl- (9CI)  (CA INDEX
     NAME)
OTHER NAMES:
CN   19: PN: WO0135984 SEQID: 19 unclaimed protein
SQL  32

SEQ      1 SRAHQHSMET RTPDINPAWY TGRGIRPVGR FG
           ========== ========== ========== =
HITS AT:   1-31

REFERENCE   1:  135:14693

REFERENCE   2:  127:118270

L1   ANSWER 19 OF 32  REGISTRY  COPYRIGHT 2002 ACS
```

RN 192588-09-3 REGISTRY
CN L-Phenylalanine, L-seryl-L-arginyl-L-alanyl-L-histidyl-L-glutaminyl-L-histidyl-L-seryl-L-methionyl-L-.alpha.-glutamyl-L-threonyl-L-arginyl-L-threonyl-L-prolyl-L-.alpha.-aspartyl-L-isoleucyl-L-asparaginyl-L-prolyl-L-alanyl-L-tryptophyl-L-tyrosyl-L-threonylglycyl-L-arginylglycyl-L-isoleucyl-L-arginyl-L-prolyl-L-valylglycyl-L-arginyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 162: PN: WO0069900 SEQID: 167 unclaimed protein
CN 18: PN: WO0135984 SEQID: 18 claimed protein
CN 3: PN: WO9960112 SEQID: 3 claimed protein
CN Protein (mouse clone pBOV3 G protein-coupled receptor ligand)
SQL 31

SEQ 1 SRAHQHSMET RTPDINPAWY TGRGIRPVGR F
========== ========== ========== =
HITS AT: 1-31

REFERENCE 1: 135:14693

REFERENCE 2: 134:21425

REFERENCE 3: 133:79323

REFERENCE 4: 132:11632

REFERENCE 5: 130:94530

REFERENCE 6: 130:91922

REFERENCE 7: 130:836

REFERENCE 8: 127:118270

L1 ANSWER 20 OF 32 REGISTRY COPYRIGHT 2002 ACS
RN 192527-01-8 REGISTRY
CN Protein (human clone pHOB7 G protein-coupled receptor ligand) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 29: PN: WO0135984 SEQID: 30 claimed protein
CN Prolactin-releasing peptide, prepro- (human)
CN Protein (human hypothalumus-derived G protein-coupled receptor ligand)
SQL 87

SEQ 1 MKVLRAWLLC LLMLGLALRG AASRTHRHSM EIRTPDINPA WYASRGIRPV
======== ========== ==========
51 GRFGRRRATL GDVPKPGLRP RLTCFPLEGG AMSSQDG
===
HITS AT: 23-53

REFERENCE 1: 135:14693

REFERENCE 2: 129:211873

REFERENCE 3: 127:118270

L1 ANSWER 21 OF 32 REGISTRY COPYRIGHT 2002 ACS
RN 192526-94-6 REGISTRY
CN Protein (rat clone pRAV3 G protein-coupled receptor ligand) (9CI) (CA INDEX NAME)

```
OTHER NAMES:
CN   16: PN: WO0135984 SEQID: 16 claimed protein
CN   GenBank AB040613-derived protein GI 13359301
CN   Prolactin-releasing factor (Rattus norvegicus strain Sprague-Dawley gene
     Prrp)
CN   Prolactin-releasing peptide, prepro- (rat)
CN   Protein (rat hypothalumus-derived G protein-coupled receptor ligand)
SQL  83

SEQ      1 MALKTWLLCL LLLSLVLPGA SSRAHQHSME TRTPDINPAW YTGRGIRPVG
                                   ========= ========== ==========
        51 RFGRRRATPR DVTGLGQLSC LPLDGRTKFS QRG
           ==
HITS AT:   22-52

REFERENCE   1:  135:191115

REFERENCE   2:  135:14693

REFERENCE   3:  129:211873

REFERENCE   4:  127:118270

L1   ANSWER 22 OF 32  REGISTRY  COPYRIGHT 2002 ACS
RN   192526-83-3  REGISTRY
CN   Protein (cattle clone pBOV3 G protein-coupled receptor ligand) (9CI)  (CA
     INDEX NAME)
OTHER NAMES:
CN   1: PN: WO0135984 SEQID: 1 claimed protein
CN   Prolactin-releasing peptide, prepro- (cattle)
CN   Protein (cattle hypothalumus-derived G protein-coupled receptor ligand)
SQL  98

SEQ      1 MKAVGAWLLC LLLLGLALQG AASRAHQHSM EIRTPDINPA WYAGRGIRPV
                                   ======== ========== ==========
        51 GRFGRRRAAP GDGPRPGPRR VPACFRLEGG AEPSRALPGR LTAQLVQE
           ===
HITS AT:   23-53

REFERENCE   1:  135:14693

REFERENCE   2:  133:79323

REFERENCE   3:  129:211873

REFERENCE   4:  127:118270

L1   ANSWER 23 OF 32  REGISTRY  COPYRIGHT 2002 ACS
RN   191919-86-5  REGISTRY
CN   L-Arginine, L-threonyl-L-prolyl-L-.alpha.-aspartyl-L-isoleucyl-L-
     asparaginyl-L-prolyl-L-alanyl-L-tryptophyl-L-tyrosyl-L-alanyl-L-seryl-L-
     arginylglycyl-L-isoleucyl-L-arginyl-L-prolyl-L-valylglycyl-L-arginyl-L-
     phenylalanylglycyl- (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   36: PN: WO0135984 SEQID: 37 unclaimed sequence
SQL  22

SEQ      1 TPDINPAWYA SRGIRPVGRF GR
           ========== ==========
```

HITS AT: 1-20

REFERENCE 1: 135:14693

REFERENCE 2: 127:118270

L1 ANSWER 24 OF 32 REGISTRY COPYRIGHT 2002 ACS
RN 191919-85-4 REGISTRY
CN Glycine, L-threonyl-L-prolyl-L-.alpha.-aspartyl-L-isoleucyl-L-asparaginyl-L-prolyl-L-alanyl-L-tryptophyl-L-tyrosyl-L-alanyl-L-seryl-L-arginylglycyl-L-isoleucyl-L-arginyl-L-prolyl-L-valylglycyl-L-arginyl-L-phenylalanyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 35: PN: WO0135984 SEQID: 36 unclaimed sequence
SQL 21

SEQ 1 TPDINPAWYA SRGIRPVGRF G
========== ==========
HITS AT: 1-20

REFERENCE 1: 135:14693

REFERENCE 2: 127:118270

L1 ANSWER 25 OF 32 REGISTRY COPYRIGHT 2002 ACS
RN 191919-84-3 REGISTRY
CN L-Phenylalanine, L-threonyl-L-prolyl-L-.alpha.-aspartyl-L-isoleucyl-L-asparaginyl-L-prolyl-L-alanyl-L-tryptophyl-L-tyrosyl-L-alanyl-L-seryl-L-arginylglycyl-L-isoleucyl-L-arginyl-L-prolyl-L-valylglycyl-L-arginyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 163: PN: WO0069900 SEQID: 166 unclaimed sequence
CN 34: PN: WO0135984 SEQID: 35 claimed sequence
CN 5: PN: WO9960112 SEQID: 5 claimed protein
SQL 20

SEQ 1 TPDINPAWYA SRGIRPVGRF
========== ==========
HITS AT: 1-20

REFERENCE 1: 135:14693

REFERENCE 2: 134:21425

REFERENCE 3: 133:79323

REFERENCE 4: 132:11632

REFERENCE 5: 127:118270

L1 ANSWER 26 OF 32 REGISTRY COPYRIGHT 2002 ACS
RN 191919-83-2 REGISTRY
CN L-Arginine, L-threonyl-L-prolyl-L-.alpha.-aspartyl-L-isoleucyl-L-asparaginyl-L-prolyl-L-alanyl-L-tryptophyl-L-tyrosyl-L-threonylglycyl-L-arginylglycyl-L-isoleucyl-L-arginyl-L-prolyl-L-valylglycyl-L-arginyl-L-phenylalanylglycyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 22: PN: WO0135984 SEQID: 23 unclaimed sequence
SQL 22

```
SEQ      1 TPDINPAWYT GRGIRPVGRF GR
           ========== ==========
HITS AT:   1-20

REFERENCE   1:  135:14693

REFERENCE   2:  127:118270

L1   ANSWER 27 OF 32  REGISTRY  COPYRIGHT 2002 ACS
RN   191919-82-1  REGISTRY
CN   Glycine, L-threonyl-L-prolyl-L-.alpha.-aspartyl-L-isoleucyl-L-asparaginyl-
     L-prolyl-L-alanyl-L-tryptophyl-L-tyrosyl-L-threonylglycyl-L-arginylglycyl-
     L-isoleucyl-L-arginyl-L-prolyl-L-valylglycyl-L-arginyl-L-phenylalanyl-
     (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   21: PN: WO0135984 SEQID: 22 unclaimed sequence
SQL  21

SEQ      1 TPDINPAWYT GRGIRPVGRF G
           ========== ==========
HITS AT:   1-20

REFERENCE   1:  135:14693

REFERENCE   2:  127:118270

L1   ANSWER 28 OF 32  REGISTRY  COPYRIGHT 2002 ACS
RN   191919-81-0  REGISTRY
CN   L-Phenylalanine, L-threonyl-L-prolyl-L-.alpha.-aspartyl-L-isoleucyl-L-
     asparaginyl-L-prolyl-L-alanyl-L-tryptophyl-L-tyrosyl-L-threonylglycyl-L-
     arginylglycyl-L-isoleucyl-L-arginyl-L-prolyl-L-valylglycyl-L-arginyl-
     (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   12: PN: WO9960112 SEQID: 13 claimed protein
CN   165: PN: WO0069900 SEQID: 168 unclaimed sequence
CN   20: PN: WO0135984 SEQID: 21 claimed sequence
SQL  20

SEQ      1 TPDINPAWYT GRGIRPVGRF
           ========== ==========
HITS AT:   1-20

REFERENCE   1:  135:14693

REFERENCE   2:  134:21425

REFERENCE   3:  133:79323

REFERENCE   4:  132:11632

REFERENCE   5:  130:91922

REFERENCE   6:  127:118270

L1   ANSWER 29 OF 32  REGISTRY  COPYRIGHT 2002 ACS
RN   191919-80-9  REGISTRY
CN   L-Arginine, L-threonyl-L-prolyl-L-.alpha.-aspartyl-L-isoleucyl-L-
     asparaginyl-L-prolyl-L-alanyl-L-tryptophyl-L-tyrosyl-L-alanylglycyl-L-
```

arginylglycyl-L-isoleucyl-L-arginyl-L-prolyl-L-valylglycyl-L-arginyl-L-phenylalanylglycyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 8: PN: WO0135984 SEQID: 8 unclaimed sequence
SQL 22

SEQ 1 TPDINPAWYA GRGIRPVGRF GR
========== ==========
HITS AT: 1-20

REFERENCE 1: 135:14693

REFERENCE 2: 127:118270

L1 ANSWER 30 OF 32 REGISTRY COPYRIGHT 2002 ACS
RN 191919-79-6 REGISTRY
CN Glycine, L-threonyl-L-prolyl-L-.alpha.-aspartyl-L-isoleucyl-L-asparaginyl-L-prolyl-L-alanyl-L-tryptophyl-L-tyrosyl-L-alanylglycyl-L-arginylglycyl-L-isoleucyl-L-arginyl-L-prolyl-L-valylglycyl-L-arginyl-L-phenylalanyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 7: PN: WO0135984 SEQID: 7 unclaimed sequence
SQL 21

SEQ 1 TPDINPAWYA GRGIRPVGRF G
========== ==========
HITS AT: 1-20

REFERENCE 1: 135:14693

REFERENCE 2: 127:118270

L1 ANSWER 31 OF 32 REGISTRY COPYRIGHT 2002 ACS
RN 191919-78-5 REGISTRY
CN L-Phenylalanine, L-threonyl-L-prolyl-L-.alpha.-aspartyl-L-isoleucyl-L-asparaginyl-L-prolyl-L-alanyl-L-tryptophyl-L-tyrosyl-L-alanylglycyl-L-arginylglycyl-L-isoleucyl-L-arginyl-L-prolyl-L-valylglycyl-L-arginyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 11: PN: WO9960112 SEQID: 12 claimed protein
CN 166: PN: WO0069900 SEQID: 170 unclaimed sequence
CN 6: PN: WO0135984 SEQID: 6 claimed sequence
SQL 20

SEQ 1 TPDINPAWYA GRGIRPVGRF
========== ==========
HITS AT: 1-20

REFERENCE 1: 135:14693

REFERENCE 2: 134:21425

REFERENCE 3: 133:79323

REFERENCE 4: 132:11632

REFERENCE 5: 130:91922

REFERENCE 6: 127:118270

L1 ANSWER 32 OF 32 REGISTRY COPYRIGHT 2002 ACS
RN 191919-77-4 REGISTRY
CN L-Phenylalanine, L-seryl-L-arginyl-L-alanyl-L-histidyl-L-glutaminyl-L-histidyl-L-seryl-L-methionyl-L-.alpha.-glutamyl-L-isoleucyl-L-arginyl-L-threonyl-L-prolyl-L-.alpha.-aspartyl-L-isoleucyl-L-asparaginyl-L-prolyl-L-alanyl-L-tryptophyl-L-tyrosyl-L-alanylglycyl-L-arginylglycyl-L-isoleucyl-L-arginyl-L-prolyl-L-valylglycyl-L-arginyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 1: PN: WO9960112 SEQID: 1 claimed protein
CN 3: PN: WO0135984 SEQID: 3 claimed sequence
CN Protein (cattle G protein-coupled receptor ligand)
SQL 31

SEQ 1 SRAHQHSMEI RTPDINPAWY AGRGIRPVGR F
========== ========== ========== =

HITS AT: 1-31

REFERENCE 1: 135:14693

REFERENCE 2: 133:79323

REFERENCE 3: 132:11632

REFERENCE 4: 130:94530

REFERENCE 5: 130:91922

REFERENCE 6: 130:836

REFERENCE 7: 127:118270

```
=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 12:05:49 ON 01 APR 2002
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FILE COVERS 1907 - 1 Apr 2002  VOL 136 ISS 14
FILE LAST UPDATED: 30 Mar 2002  (20020330/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

CAS roles have been modified effective December 16, 2001. Please
check your SDI profiles to see if they need to be revised. For
information on CAS roles, enter HELP ROLES at an arrow prompt or use
the CAS Roles thesaurus (/RL field) in this file.

The P indicator for Preparations was not generated for all of the
CAS Registry Numbers that were added to the CAS files between 12/27/01
and 1/23/02.  As of 1/23/02, the situation has been resolved.  Searches
and/or SDIs in the H/Z/CA/CAplus files incorporating CAS Registry
Numbers with the P indicator executed between 12/27/01 and 1/23/02 may
be incomplete.  See the NEWS message on this topic for more information.

=>
=>
=> d stat que
L1            32 SEA FILE=REGISTRY ABB=ON  PLU=ON  TPDINPAWYXXRGIRPVGRFXX|SRAHQH
                 SMEIRTPDINPAWYAGRGIRPVGRF|TPDINPAWYAGRGIRPVGRF|SRAHQHSMETRTPDIN
                 PAWYTGRGIRPVGRF|TPDINPAWYTGRGIRPVGRF|SRTHRHSMEIRTPDINPAWYASRGIR
                 PVGRF|TPDINPAWYASRGIRPVGRF/SQSP
L2            25 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L1
L3            85 SEA FILE=REGISTRY ABB=ON  PLU=ON  G-PROTEIN?/CN
L4          1103 SEA FILE=REGISTRY ABB=ON  PLU=ON  LIGAND(L)(POLYPEPTIDE OR
                 PEPTIDE OR PROTEIN)
L5           584 SEA FILE=REGISTRY ABB=ON  PLU=ON  PROLACTIN/BI
L6         43103 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3 OR G(W)PROTEIN?
L7         56928 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L4 OR LIGAND(L)(POLYPEPTIDE
                 OR PEPTIDE OR PROTEIN)
L8         67365 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L5 OR ?PROLACT?
L9          3473 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L6(L)L7
L10           28 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9 AND L8
L11           20 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L10 NOT L2


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L11 ANSWER 1 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:171404 HCAPLUS
TITLE: The Effects of Centrally Administered Apelin-13 on Food Intake, Water Intake and Pituitary Hormone Release in Rats
AUTHOR(S): Taheri, Shahrad; Murphy, Kevin; Cohen, Mark; Sujkovic, Elizabeth; Kennedy, Adam; Dhillo, Waljit; Dakin, Catherine; Sajedi, Arshia; Ghatei, Mohammad; Bloom, Stephen
CORPORATE SOURCE: Endocrine Unit, Imperial College School of Medicine, Hammersmith Hospital, London, W12 0NN, UK
SOURCE: Biochemical and Biophysical Research Communications (2002), 291(5), 1208-1212
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Apelin is the recently identified endogenous ligand for the G-protein-coupled receptor, APJ. Preproapelin and APJ mRNA are found in hypothalamic regions known to be important in the regulation of food and water intake, and pituitary hormone release. The effects of intracerebroventricular (ICV) administration of pyroglutamylated apelin-13 on food and water intake and pituitary hormone release in rats were investigated. Apelin-13 had little effect on food intake, but dose-dependently increased drinking behavior and water intake at 1 h. Apelin-13 (10 nmol) increased water intake by up to sixfold compared to saline. Compared to saline control, apelin-13 (10 nmol) significantly increased plasma ACTH and corticosterone and decreased plasma prolactin, LH and FSH at 30 min. In vitro, apelin-13 stimulated the release of CRH and AVP from hypothalamic explants, but had no effect on NPY release. These results suggest that apelin may play an important role in the hypothalamic regulation of water intake and endocrine axes. (c) 2002 Academic Press.

L11 ANSWER 2 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:935785 HCAPLUS
DOCUMENT NUMBER: 136:65196
TITLE: cDNA and protein sequences of Ligands to G protein -coupled receptor 8 GPR8 and their used in drug screening, diagnosis and therapeutics
INVENTOR(S): Mori, Masaaki; Shimomura, Yukio; Harada, Mioko; Kurihara, Mika; Kitada, Chieko; Asami, Taiji; Matsumoto, Yoshio; Adachi, Yuka; Watanabe, Takuya; Sugo, Tsukasa; Abe, Michiko
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd, Japan
SOURCE: PCT Int. Appl., 221 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001098494	A1	20011227	WO 2001-JP5257	20010620

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS,
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,
RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2000-191089 A 20000621
JP 2000-275013 A 20000906
JP 2001-116000 A 20010413

AB This invention provides cDNA and **protein** sequences of **ligands** to **G protein**-coupled receptor 8 GPR8 clone from human, pig and mouse and rat. The binding of **ligands** to GPR8 expressed on CHO cell repressed the synthesis of cAMP in the cell. The GPR8 **ligands** provides in this invention can be used in drug screening, diagnosis and therapeutics for development of antiobesity agents, appetite stimulants and **prolactin** prodn. inhibitor.

IT **383450-05-3 383450-15-5 383450-17-7**
383450-21-3 383450-25-7
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence of GPR8 **ligand**; cDNA and **protein** sequences of **Ligands** to **G protein**-coupled receptor 8 GPR8 and their used in drug screening, diagnosis and therapeutics)

IT **9002-62-4, Prolactin**, biological studies
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of, GPR8 **ligand** for; cDNA and **protein** sequences of **Ligands** to **G protein**-coupled receptor 8 GPR8 and their used in drug screening, diagnosis and therapeutics)

IT **383449-51-2 383450-06-4 383450-07-5**
383450-08-6 383450-09-7 383450-10-0
383450-11-1 383450-12-2 3B3450-13-3
383450-14-4 383450-16-6 383450-18-8
383450-19-9 383450-20-2 383450-22-4
383450-23-5 383450-24-6 383450-26-8
383450-27-9 383450-28-0 383450-29-1
383450-30-4 383450-31-5 383450-32-6
383450-33-7 383450-34-8 383450-35-9
383450-36-0 383450-37-1
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleotide sequence; cDNA and **protein** sequences of **Ligands** to **G protein**-coupled receptor 8 GPR8 and their used in drug screening, diagnosis and therapeutics)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:798398 HCAPLUS
DOCUMENT NUMBER: 135:353691
TITLE: Yeast cell systems expressing heterologous fused proteins and methods of screening for compounds having peptide-binding activity
INVENTOR(S): Young, Kathleen H.; Cao, Jian
PATENT ASSIGNEE(S): American Home Products Corporation, USA

SOURCE: PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001081548	A1	20011101	WO 2001-US13006	20010423

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-556390 A 20000424

AB This invention relates to novel modified yeast host cells which express heterologous fused proteins and methods of screening for test samples having peptide-binding activity such as ligands and receptors. The modified host cell comprises: (a) a gene sequence encoding a heterologous fusion protein comprised of a first peptide (e.g. a ligand), which is joined to the DNA binding domain of a transcriptional activation protein; (b) a gene sequence encoding a heterologous fusion protein comprised of a second peptide (e.g. a corresponding receptor), which is joined to the transcriptional activation domain of a transcriptional activation protein; wherein binding of the first and second peptides reconstitutes a transcriptional activation protein; (c) a gene encoding a reporter luciferase, which is under pos. control of the reconstituted transcriptional activation protein; and (d) optionally, a deletion or mutation in the chromosomal DNA of the host cell for the transcriptional activation protein if present in the selected host cell. The method was demonstrated by the expression of peptide binding pairs, e.g., **prolactin-prolactin** receptor and growth hormone-growth hormone receptor, in Saccharomyces cerevisiae.

IT **9002-62-4**, **Prolactin**, biological studies
9035-54-5, Placental lactogen
RL: BUU (Biological use, unclassified); BIDL (Biological study); USES (Uses)
(yeast cell systems screening for compds. having peptide-binding activity expressing heterologous fused proteins contg.)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:473619 HCAPLUS
DOCUMENT NUMBER: 135:190715
TITLE: Identification of G protein-coupled, inward rectifier potassium channel gene products from the rat anterior pituitary gland
AUTHOR(S): Gregerson, Karen A.; Flagg, Thomas P.; D'Neill, Thomas J.; Anderson, Mark; Lauring, Danh; Horel, Jill S.; Welling, Paul A.
CORPORATE SOURCE: Departments of Obstetrics, Gynecology, Sciences and Physiology and the Center for Studies in Reproduction, University of Maryland, Baltimore, MD, 21201, USA

SOURCE: Endocrinology (2001), 142(7), 2820-2832
CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Dopamine (DA) is a physiol. regulator of PRL secretion, exerting tonic inhibitory control. DA activates an inward rectifier K+ (IRK) channel in rat lactotrophs, causing membrane hyperpolarization and inhibition of Ca2+-dependent action potentials. Both the activation of this effector K+ channel and the inhibition of PRL release are mediated by D2-type receptor activation and pertussis toxin-sensitive **G proteins**.
To study the mol. basis of this physiol. relevant channel, a homol.-based PCR approach was employed to identify members of the IRK channel family expressed in the anterior pituitary gland. Nondegenerate primers corresponding to regions specific for IRK channels known to be **G protein** activated (GIRKs; gene subfamily Kir 3.0) were synthesized and used in the PCR with reverse transcribed female rat anterior pituitary mRNA as the template. PCR products of predicted sizes for Kir 3.1, 3.2, and 3.4 were consistently obsd. by ethidium bromide staining after 16 amplification cycles. The identities of the products were confirmed by subcloning and sequencing. Expression of each of these gene products in anterior pituitary was confirmed by Northern blot anal. Functional anal. of the GIRK **proteins** was performed in the heterologous expression system, Xenopus laevis oocytes. Macroscopic K+ currents were examd. in oocytes injected with different combinations of Kir 3.0 complementary RNA (cRNA) and **G protein** subunit (.beta.1.gamma.2) cRNA. The current-voltage relationships demonstrated strong inward rectification for each individual and pairwise combination of GIRK channel subunits. Oocytes coinjected with any pair of GIRK subunit cRNA exhibited significantly larger inward K+ currents than oocytes injected with only one GIRK channel subtype. **Ligand**-dependent activation of only one of the GIRK combinations (GIRK1 and GIRK4) was obsd. when channel subunits were co-expressed with the D2 receptor in Xenopus oocytes. Dose-response data fit to a Michaelis-Menten equation gave an apparent Kd similar to that for DA binding in anterior pituitary tissue. GIRK1 and GIRK4 **proteins** were coimmunopptd. from anterior pituitary lysates, confirming the presence of native GIRK1/GIRK4 oligomers in this tissue. These data indicate that GIRK1 and GIRK4 are excellent candidate subunits for the D2-activated, **G protein**-gated channel in pituitary lactotrophs, where they play a crit. role in excitation-secretion coupling.

IT **9002-62-4, Prolactin**, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(identification of G protein-coupled, inward rectifier potassium channel gene products from rat anterior pituitary gland)

REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 5 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:350675 HCAPLUS
DOCUMENT NUMBER: 134:336289
TITLE: **Prolactin**-releasing peptide
AUTHOR(S): Hinuma, Shuji
CORPORATE SOURCE: Discovery Res. Lab. I, Pharm. Discovery Res. Div., Takeda Chem. Ind., Ltd., Japan
SOURCE: Horumon to Rinsho (2001), 49(4), 377-385
CODEN: HORIAE; ISSN: 0045-7167
PUBLISHER: Igaku no Sekaisha

DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review with 37 refs., on novel bioactive **peptide**, **prolactin** releasing **peptide** (PrRP), isolated as a **ligand** for orphan G **protein**-coupled receptors (GPCR), discussing cloning of hGR3, a novel human GPCR, and its structure, discovery of PrRP as a lignd for hGR, tissue distribution of PrRP and its receptors, and physiol. functions of PrRP, including promoting effects on secretion of **prolactin**, oxytocin, GH-releasing factor, and GnRH, hypertensive action, food intake regulatory function. Receptor-mediated signal transduction of PrRP is also discussed.
IT **39362-14-6**, **Prolactin**-releasing factor
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(structure, distribution, and functions of **prolactin** -releasing **peptide** as a **ligand** for orphan G **protein**-coupled receptors)

L11 ANSWER 6 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:911416 HCAPLUS
DOCUMENT NUMBER: 134:66713
TITLE: Rat brain .gamma.-hydroxybutyrate receptor and cDNA and methods of drug screening and diagnosis and treatment of diseases
INVENTOR(S): Andriamanpandry, Christian; Maitre, Michel
PATENT ASSIGNEE(S): Universite Louis Pasteur, Fr.
SOURCE: PCT Int. Appl., 66 pp.
COOEN: PIXX02
OOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KINO	OATE	APPLICATION NO.	OATE
WO 2000078948	A2	20001228	WO 2000-FR1687	20000619
WO 2000078948	A3	20010301		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TO, TG

FR 2795075	A1	20001222	FR 1999-7784	19990618

PRIORITY APPLN. INFO.: FR 1999-7784 A 19990618
AB The invention concerns a novel .gamma.-hydroxybutyrate (GHB) receptor characterized by it functional activities, the cloning of the cONA coding for said receptor, vectors and transformed cells, and methods for selecting compds. useful as medicine for preventing and/or treating pathologies assocd. directly or indirectly with the activity of said receptor or its natural **ligand**, GHB. Thus, rat brain GHB receptor cONA was cloned and sequenced. The 56-kilodalton, G **protein**-coupled receptor contains 7 transmembrane domains, glycosylation sites, and sites for phosphorylation by **protein**

kinases A, C, and G and by casein kinase II. The receptor binds GHB with high affinity (Kd = 425 nM) and also binds trans-4-hydroxycrotonate and p-chlorophenyl-trans-hydroxycrotonate, but does not bind GABA, glutamate, nor baclofen.

IT **9002-62-4, Prolactin**, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(regulation of secretion of; rat brain .gamma.-hydroxybutyrate receptor and cDNA and methods of drug screening and diagnosis and treatment of diseases)

L11 ANSWER 7 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:910829 HCAPLUS
DOCUMENT NUMBER: 134:157852
TITLE: Identification and characterization of two G protein-coupled receptors for neuropeptide FF
AUTHOR(S): Bonini, James A.; Jones, Kenneth A.; Adham, Nika; Forray, Carlos; Artymyshyn, Roman; Durkin, Margaret M.; Smith, Kelli E.; Tamm, Joseph A.; Boteju, Lakmal W.; Lakhlani, Parul P.; Raddatz, Rita; Yao, Wen-Jeng; Ogozalek, Kristine L.; Boyle, Noel; Kouranova, Evguenia V.; Quan, Yong; Vaysse, Pierre J.; Wetzel, John M.; Branchek, Theresa A.; Gerald, Christophe; Borowsky, Beth
CORPORATE SOURCE: Synaptic Pharmaceutical Corporation, Paramus, NJ, 07652, USA
SOURCE: Journal of Biological Chemistry (2000), 275(50), 39324-39331
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The central nervous system octapeptide, neuropeptide FF (NPFF),is believed to play a role in pain modulation and opiate tolerance. Two G **protein**-coupled receptors, NPFF1 and NPFF2, were isolated from human and rat central nervous system tissues. NPFF specifically bound to NPFF1 (Kd = 1.13 nM) and NPFF2 (Kd = 0.37 nM), and both receptors were activated by NPFF in a variety of heterologous expression systems. The localization of mRNA and binding sites of these receptors in the dorsal horn of the spinal cord, the lateral hypothalamus, the spinal trigeminal nuclei, and the thalamic nuclei supports a role for NPFF in pain modulation. Among the receptors with the highest amino acid sequence homol. to NPFF1 and NPFF2 are members of the orexin, NPY, and cholecystokinin families, which have been implicated in feeding. These similarities together with the finding that BIBP3226, an anorexigenic Y1 receptor **ligand**, also binds to NPFF1 suggest a potential role for NPFF1 in feeding. The identification of NPFF1 and NPFF2 will help delineate their roles in these and other physiol. functions.

IT **263096-44-2**
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(amino acid sequence; identification, characterization, tissue and chromosomal localization, and function of two G protein-coupled receptors for neuropeptide FF)

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 8 OF 20 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:351557 HCAPLUS
DOCUMENT NUMBER: 133:16312
TITLE: Novel **G protein**-coupled receptor **protein**, its DNA and **ligand** thereof
INVENTOR(S): Watanabe, Takuya; Kikuchi, Kuniko; Terao, Yasuko; Shintani, Yasushi; Hinuma, Shuji; Fukusumi, Shoji; Fujii, Ryo; Hosoya, Masaki; Kitada, Chieko
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 184 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000029441	A1	20000525	WO 1999-JP6283	19991111
W: AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CR, CU, CZ, DM, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MA, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1132405	A1	20010912	EP 1999-972224	19991111
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2001149072	A2	20010605	JP 1999-323017	19991112

PRIORITY APPLN. INFO.:

JP 1998-323759	A	19981113
JP 1999-60030	A	19990308
JP 1999-106812	A	19990414
JP 1999-166672	A	19990614
JP 1999-221640	A	19990804
JP 1999-259818	A	19990914
WO 1999-JP6283	W	19991111

AB A novel polypeptide, its peptide fragments or salts thereof; a process for producing this polypeptide; a receptor of the polypeptide; drugs contg. the polypeptide, etc.; an antibody against the polypeptide; a method/kit for screening compds. promoting or inhibiting the activity of the polypeptide; the compds. obtained by the screening; and drugs, etc. contg. these compds. The above polypeptide or its peptide fragments are usable as, for example, remedies for nervous diseases and somatostatin excretion promoters. The above antibody is usable in, for example, quantitating the polypeptide in a liq. specimen. Further, the polypeptide is useful as a reagent for screening the compds. promoting or inhibiting the activity of the polypeptide.

IT **263096-44-2 271564-72-8 271564-74-0**
271564-76-2 271564-78-4 271564-80-8
271564-86-4
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; novel **G protein**-coupled receptor **protein**, its DNA and **ligand** and use for treating nervous diseases and as somatostatin excretion promoters)

IT **271564-73-9 271564-75-1 271564-77-3**
271564-79-5 271564-81-9 271564-83-1
271564-84-2

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; novel G protein-coupled receptor protein, its DNA and ligand and use for treating nervous diseases and as somatostatin excretion promoters)
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 9 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:684421 HCAPLUS
DOCUMENT NUMBER: 132:88228
TITLE: Discovery of novel peptide ligands , prolactin releasing peptide (PrRP) and Apelin for orphan G protein-coupled receptors
AUTHOR(S): Onda, Haruo; Fujino, Masahiko
CORPORATE SOURCE: Discovery Res. Lab. 1, Pharm. Discovery Res. Div. Takeda Chem. Ind., LTD., Tsukuba, 300-4293, Japan
SOURCE: Naibunpi, Tonyobyoka (1999), 8(6), 595-601
CODEN: NATOFF; ISSN: 1341-3724
PUBLISHER: Kagaku Hyoronsha
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review with 10 refs., on prepn. of orphan receptors and searching and purifn. of peptide ligands, esp. PrRP and apelin.
IT 39362-14-6, Prolactin-releasing factor
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); PRP (Properties); BIOL (Biological study); PROC (Process)
(discovery of novel peptide ligands, prolactin releasing peptide and apelin for orphan G protein-coupled receptors)

L11 ANSWER 10 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:447438 HCAPLUS
DOCUMENT NUMBER: 131:111510
TITLE: A novel natural ligand for orphan G -protein coupled receptor. Finding prolactin releasing peptide (PrRP)
AUTHOR(S): Onda, Haruo; Fujino, Masahiko
CORPORATE SOURCE: Pharm. Discovery Res. Div., Takeda Chem. Ind., Tsukuba, 300-4293, Japan
SOURCE: Seikagaku (1999), 71(6), 448-454
CODEN: SEIKAQ; ISSN: 0037-1017
PUBLISHER: Nippon Seikagakkai
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review with 14 refs., on (1) the importance of orphan G-protein coupled receptors (GPCRs) and their ligands in the development of novel drugs in reverse pharmacol., (2) search strategy for the natural ligands of GPCRs by using gene technol. and protein chem., and (3) isolation of PrRP from hypothalamus and its structure and physiol. functions.

L11 ANSWER 11 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:778901 HCAPLUS
DOCUMENT NUMBER: 130:122420
TITLE: The Lymnaea cardioexcitatory peptide (LyCEP) receptor: a G-protein-coupled receptor for a novel member of the RFamide neuropeptide family

AUTHOR(S): Tensen, Cornelis P.; Cox, Kingsley J. A.; Smit, August B.; Van Der Schors, Roel C.; Meyerhof, Wolfgang; Richter, Dietmar; Planta, Rudi J.; Hermann, Petra M.; Van Minnen, Jan; Geraerts, Wijnand P. M.; Knol, Jaco C.; Burke, Julian F.; Vreugdenhil, Erno; Van Heerikhuizen, Harm

CORPORATE SOURCE: Departments of Biochemistry and Molecular Biology and Molecular Neurobiology, Research Institute Neurosciences, Vrije Universiteit, Amsterdam, 1081 HV, Neth.

SOURCE: J. Neurosci. (1998), 18(23), 9812-9821
CODEN: JNRSDS; ISSN: 0270-6474

PUBLISHER: Society for Neuroscience

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A novel **G-protein**-coupled receptor (GRL106) resembling neuropeptide Y and tachykinin receptors was cloned from the mollusk L. stagnalis. Application of a **peptide** ext. from the Lymnaea brain to Xenopus oocytes expressing GRL 106 activated a calcium-dependent chloride channel. Using this response as a bioassay, we purified the **ligand** for GRL106, Lymnaea cardioexcitatory **peptide** (LyCEP), an RFamide-type decapeptide (TPHWRPQGRF-NH2) displaying significant similarity to the Achatina cardioexcitatory **peptide** (ACEP-1) as well as to the recently identified family of mammalian **prolactin**-releasing **peptides**. In the Lymnaea brain, the cells that produce egg-laying hormone are the predominant site of GRL106 gene expression and appear to be innervated by LyCEP-contg. fibers. Indeed, LyCEP application transiently hyperpolarizes isolated egg-laying hormone cells. In the Lymnaea pericardium, LyCEP-contg. fibers end blindly at the pericardial lumen, and the heart is stimulated by LyCEP in vitro. These data confirm that LyCEP is an RFamide **ligand** for GRL106.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 12 OF 20 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:550435 HCAPLUS

DOCUMENT NUMBER: 129:171503

TITLE: Library screening as a strategy to clone drugs for G protein-coupled receptors

INVENTOR(S): Gershengorn, Marvin C.; Geras-Raaka, Elizabeth; Nussenzveig, Daniel R.

PATENT ASSIGNEE(S): Cornell Research Foundation, Inc., USA

SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9834948	A1	19980813	WO 1998-US2377	19980205

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI,

FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9861498	A1	19980826	AU 1998-61498	19980205
EP 1015478	A1	20000705	EP 1998-906219	19980205
R: DE, FR, GB, IT				

PRIORITY APPLN. INFO.: US 1997-795876 A 19970206
WO 1998-US2377 W 19980205

AB The present invention is directed to a strategy to identify small **peptides** that activate any **G protein**-coupled receptor (GPCR) or inactivate any constitutively active GPCR by screening combinatorial **peptide** libraries. The invention comprises expressing a **peptide** of a **peptide** library tethered to a GPCR of interest in a cell, and monitoring the cell to det. whether the **peptide** is an agonist or neg. antagonist of the GPCR of interest. The **peptide** is tethered to the GPCR by replacing the amino terminus of the GPCR with the amino terminus of a self-activating receptor, and replacing the natural **peptide ligand** present in the amino terminus with the library **peptide**. In one embodiment for discovery of agonists, a **ligand** of the self-activating receptor is used to cleave the resulting amino terminus to expose the **peptide** of the **peptide** library. In another embodiment for discovery of agonists or neg. antagonists, the GPCR construct ends in the **peptide** so the **peptide** is always exposed. Preferably, the self-activating receptor is the thrombin receptor and the **ligand** of the self-activating receptor is thrombin.

IT **211485-84-6P**
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); BIOL (Biological study); PREP (Preparation); USES (Uses)
(library screening as strategy to clone drugs for G protein-coupled FSH receptors)

IT **211485-95-9P**
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); BIOL (Biological study); PREP (Preparation); USES (Uses)
(library screening as strategy to clone drugs for G protein-coupled calcitonin receptors)

L11 ANSWER 13 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:650247 HCAPLUS
DOCUMENT NUMBER: 127:314833
TITLE: Selective target cell activation by expression of a **G protein**-coupled receptor activated superiorly by synthetic **ligand**
INVENTOR(S): Conklin, Bruce R.
PATENT ASSIGNEE(S): Regents of the University of California, USA; Conklin, Bruce R.
SOURCE: PCT Int. Appl., 117 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9735478	A1	19971002	WO 1997-US5334	19970325
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL,				

PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9724308	A1	19971017	AU 1997-24308 19970325
EP 893950	A1	19990203	EP 1997-920009 19970325

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

PRIORITY APPLN. INFO.: US 1996-622348 19960326
WO 1997-US5334 19970325

AB The invention provides a method for selectively activating a target cell, where the target cell expresses a receptor activated superiorly by a synthetic **ligand** (RASSL) having decreased binding affinity for a selected natural **ligand** and normal or near normal binding affinity for a synthetic small mol. agonist. Thus, RASSL-mediated activation of target cells does not occur to a significant extent in the presence of natural **G protein**-coupled receptor **ligand**, but is significantly stimulated upon exposure to a synthetic small mol. RASSL-expressing target cells are selectively activated by exposing of the cells to an appropriate synthetic small mol., which in turn binds the RASSL, resulting in **G protein** activation and triggering of a specific cellular response assocd. with **G protein** activation (e.g., cellular proliferation or cellular secretion).

IT **197665-27-3P 197665-29-5P**
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BPN (Biosynthetic preparation); BPR (Biological process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process); USES (Uses)
(amino acid sequence; selective target cell activation by expression of a **G protein**-coupled receptor activated superiorly by synthetic **ligand**)

IT **197665-26-2P 197665-28-4P**
RL: BOC (Biological occurrence); BPN (Biosynthetic preparation); PRP (Properties); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation)
(nucleic acid sequence; selective target cell activation by expression of a **G protein**-coupled receptor activated superiorly by synthetic **ligand**)

L11 ANSWER 14 OF 20 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:	1997:434125 HCAPLUS
DOCUMENT NUMBER:	127:130772
TITLE:	Lovastatin decreases **prolactin** and growth hormone gene expression in GH4C1 cells through a cAMP dependent mechanism
AUTHOR(S):	Lasa, Marina; Chiloeches, Antonio; Garcia, Natalia; Montes, Agustin; Toro, Maria J.
CORPORATE SOURCE:	Dep. Bioquimica Biologia Mol., Univ. Alcala. Ctra. Madrid-Barcelona Km 33600, Madrid, 28871, Spain
SOURCE:	Mol. Cell. Endocrinol. (1997), 130(1,2), 93-100 CODEN: MCEND6; ISSN: 0303-7207
PUBLISHER:	Elsevier
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB The heterotrimeric **G protein** Gs couples several surface **ligand** receptors to cAMP prodn., as well as to both growth hormone (GH) and **prolactin** (PRL) gene expression in

pituitary and GH cells. It has been shown that constitutively active .alpha.s stimulates transient expression of both PRL- and GH-chloramphenicol acetyl transferase (CAT) constructions, which indicates that both the PRL and GH promoter regions are under the influence of signal pathways mediated by .alpha.s. We have previously shown that the cholesterol lowering drug lovastatin decreases both the amt. of G.alpha.s subunit in the membrane and the adenylyl cyclase activity in GH4C1 cells. Thus, we tried to verify whether that decrease in .alpha.s levels could affect PRL and GH secretion, as well as the expression of PRL- and GH-CAT constructions. Since the regulation of these two genes is dependent on the pituitary specific transcription factor Pit-1, the effect of lovastatin on the expression of Pit-1-CAT constructions was also studied. Our results show that lovastatin decreased the basal expression of these three cAMP-responsive genes in GH4C1 cells, being partially reversed by the addn. of mevalonate to the culture medium. This effect of lovastatin on the promoter activities of the transfected constructions was also obsd. in PRL and GH secretion to the medium, suggesting that this drug produces similar changes in the endogenous promoters of both hormones. Moreover, the presence of lovastatin did not prevent the response to the cAMP activator forskolin, indicating that the main effect of this drug could be exerted through upstream adenylyl cyclase. In conclusion, our data indicate that lovastatin decreases the basal expression of Pit-I and consequently of both GH and PRL genes through a mechanism probably mediated by the decrease of G.alpha.s levels in the cell membrane. Taken together, these results suggest that the activity of membrane heterotrimeric **G proteins** regulates the basal transcription of specific cellular genes in GH4C1 cells. Moreover the effects of lovastatin may be taken into account in the study of constitutively endocrine disorders assocd. with an increased secretion of either PRL or GH.

IT **9002-62-4, Prolactin**, biological studies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(lovastatin decreases **prolactin** and growth hormone gene expression in GH4C1 cells through a cAMP dependent mechanism)

L11 ANSWER 15 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:239382 HCAPLUS
DOCUMENT NUMBER: 126:304326
TITLE: Galanin receptors: involvement in feeding, pain, depression and Alzheimer's disease
AUTHOR(S): Kask, Kalev; Berthold, Malin; Bartfai, Tamas
CORPORATE SOURCE: Dep. Neurochem. and Neurotoxicology, Stockholm Univ., Stockholm, S-106 91, Swed.
SOURCE: Life Sci. (1997), 60(18), 1523-1533
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 110 refs. Galanin, a neuroendocrine peptide with a multitude of functions, binds to and acts on specific G-protein coupled receptors. Only one galanin receptor subtype, GalR1, has been cloned so far, although pharmacol. evidence suggests the presence of more than one galanin receptor subtype. These receptors mediate via different Gi/Go-**proteins** the inhibition of adenylyl cyclase, opening of K+-channels and closure of Ca2+-channels. Galanin inhibits secretion of insulin, acetylcholine, serotonin and noradrenaline, while it stimulates **prolactin** and growth hormone release. Detn. of structural components of galanin receptors required for binding of the **peptide ligand** as carried out recently will facilitate

the screening and design of mols. specifically acting on galaninergic systems with therapeutic potential in Alzheimer's disease, feeding disorders, pain and depression.

L11 ANSWER 16 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:182931 HCAPLUS
DOCUMENT NUMBER: 124:221063
TITLE: Role of guanine nucleotide-binding proteins, Gi.alpha.3 and Gs.alpha., in dopamine and thyrotropin-releasing hormone signal transduction: evidence for competition and commonality
AUTHOR(S): Kineman, R. D.; Gettys, T. W.; Frawley, L. S.
CORPORATE SOURCE: Dep. Cell Biol. Anatomy, Med. Univ. South Carolina, Charleston, SC, USA
SOURCE: J. Endocrinol. (1996), 148(3), 447-55
CODEN: JOENAK; ISSN: 0022-0795
DOCUMENT TYPE: Journal
LANGUAGE: English

AB It is clear that dopamine (DA) at high concns. (>100 nmol/L) inhibits the release of **prolactin** (PRL). Paradoxically, this monoamine at low concns. (<10 nmol/L) has also been shown to augment PRL secretion. One possible explanation for these divergent effects is that DA binds receptors capable of interacting with multiple **G protein** subtypes that recruit opposing intracellular signaling pathways within lactotrophs. To identify **G proteins** which couple DA receptor activation to PRL secretion, we have selectively immunoneutralized the activity of Gi.alpha.3 and Gs.alpha. in primary cultures of rat pituitaries and subseguently tested the ability of these cultures to respond to high and low dose DA. Specifically, permeabilized pituitary cell cultures from random-cycling female rats were treated with control Igs (IgGs; 50 .mu.g/mL) purified from preimmune serum (PII) or IgGs directed against the C-terminal portion of Gi.alpha.3 or Gs.alpha.. After immunoneutralization of these **G proteins**, cells were challenged with 10 or 1000 nmol DA/L and the relative amt. of PRL released was assessed by reverse hemolytic plague assay. Results were expressed as % of basal values and compared. Under control conditions (PII), 1000 nmol DA/L inhibited (61.4% of basal values) while 10 nmol DA/L augmented (120.0%) PRL release in five sep. expts. Treatment of cells with anti-Gi.alpha.3 attenuated the inhibitory effect of high dose DA (87.3%). However, elimination of Gi.alpha.3 activity did not significantly alter the PRL stimulatory effect of 10 nmol DA/L (121.0%). Interestingly, immunoneutralization of Gs.alpha. resulted in a reciprocal shift in the activity of the lower dose of DA from stimulatory to inhibitory (69.7%) while combined treatment of anti-Gi.alpha.3 and anti-Gs.alpha. abrogated the responsiveness of pituitary cell cultures to either DA treatment (1000 nmol/L, 70.7% and 10 nmol/L, 87.5%). These data reveal that **ligand**-activated DA receptors can interact with both Gi.alpha.3 and Gs.alpha.. Elimination of the stimulatory component (Gs.alpha.) favors the DA receptor activation of the inhibitory pathway (Gi.alpha.3) suggesting a competition between neg. and pos. intracellular signaling mechanisms in normal lactotrophs. In addn. to DA treatment, we also challenged permeabilized pituitary cells with 100 nmol TSH-releasing hormone (TRH)/L as a pos. control for secretory integrity. As anticipated, TRH stimulated PRL release to 188.0% of basal values under control conditions. Unexpectedly, immunoneutralization of Gs.alpha. completely blocked the ability of TRH to induce PRL release (101.8%). This neutralizing effect was specific to Gs.alpha. in that blockade of Gi.alpha.3 activity had no significant effect on TRH-stimulated PRL release (166.2%). These data are the first to support a direct role of

Gs.alpha. in TRH signal transduction within PRL-secreting cells.
IT 9002-62-4, **Prolactin**, biological studies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(release; G proteins Gi.alpha.3 and Gs.alpha. roles in dopamine and TRH signal transduction in lactotroph)

L11 ANSWER 17 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:113481 HCAPLUS
DOCUMENT NUMBER: 124:137837
TITLE: Host cells transformed with fusion protein gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities
INVENTOR(S): Young, Kathleen H.; Ozenberger, Bradley A.
PATENT ASSIGNEE(S): American Cyanamid Co., USA
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9534646	A1	19951221	WO 1995-US6895	19950531
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TT, UA, UG, UZ, VN				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5989808	A	19991123	US 1994-259609	19940614
CA 2195083	AA	19951221	CA 1995-2195083	19950531
AU 9526066	A1	19960105	AU 1995-26066	19950531
AU 706173	B2	19990610		
EP 765389	A1	19970402	EP 1995-920689	19950531
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
ZA 9504892	A	19960130	ZA 1995-4892	19950613
LT 4230	B	19971027	LT 1997-4	19970113
LV 11906	B	19980620	LV 1997-4	19970214
US 6251602	B1	20010626	US 1999-263944	19990308
US 6284519	B1	20010904	US 1999-305483	19990506

PRIORITY APPLN. INFO.: US 1994-259609 A 19940614
WO 1995-US6895 W 19950531

AB This invention relates to novel modified host cells which express heterologous fused proteins and methods of screening for test samples having peptide-binding activity; wherein the modified host cell comprises: (a) a gene sequence encoding a heterologous fusion protein; said fusion protein comprising a first peptide of a peptide binding pair, or segment of said first peptide, which is joined to either a DNA binding domain or its corresponding transcriptional activation domain of a transcriptional activation protein; (b) a gene sequence encoding a heterologous fusion protein, said fusion protein comprising a second peptide of the peptide binding pair in (a), or a segment thereof, fused to either a DNA binding domain or its corresponding transcriptional activation domain, whichever one is not employed in (a); (c) a reporter gene operatively assocd. with the transcriptional activation protein, or a portion thereof; (d) optionally, a deletion or mutation in the chromosomal DNA of the host cell for the transcriptional activation protein if present in the selected host cell.

IT 9002-62-4, Prolactin, biological studies
RL: ANT (Analyte); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(host cells transformed with fusion protein gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)
IT 9035-54-5, Placental lactogen
RL: ANT (Analyte); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(peptide ligand; host cells transformed with fusion protein gene and method for screening test samples with receptor-ligand interactions or peptide-binding activities)

L11 ANSWER 18 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:70438 HCAPLUS
DOCUMENT NUMBER: 124:106908
TITLE: Effects of Asn318 and Asp87Asn318 mutations on signal transduction by gonadotropin-releasing hormone receptor and receptor regulation
AUTHOR(S): Awara, Wageh M.; Guo, Chuan-Hai; Conn, P. Michael
CORPORATE SOURCE: Oregon Reg. Primate Res. Cent., Beaverton, OR, 97006, USA
SOURCE: Endocrinology (1996), 137(2), 655-62
CODEN: ENDOAO; ISSN: 0013-7227
DOCUMENT TYPE: Journal
LANGUAGE: English
AB GnRH receptor (GnRH-R) contains Asn87 and Asp318 instead of the more frequently obsd. Asp87 and Asn318 found in other **G protein**-coupled receptors. In the present study, site-directed mutagenesis was used to introduce Asn318 and Asp87Asn318 into GnRH-R. The effect on coupling and regulation of GnRH-R was studied by stable expression of wild and mutant mouse GnRH-R in the lactotropic GH3 cells; these normally release PRL in response to TRH stimulation. The responses to Buserelin (a metabolically stable GnRH analog) in three different cell lines, M1, N8, and ND1 (expressing wild-type, Asn318 mutant, and Asp87Asn318 mutant mouse GnRH-R, resp.) were compared with that obsd. in the previously characterized GGH3-1' cells, which stably express rat GnRH-R. The Asn318 and Asp87Asn318 mutations had no measurable effect on **ligand** binding, but abolished the initial down-regulation of receptor that was obsd. in M1 and GGH3-1' cells, suggesting that the normal location of Asn87 and Asp318 in GnRH-R is involved in the regulation of GnRH-R. In N8 and ND1 cells, Buserelin-stimulated inositol phosphate (IP) prodn. was attenuated, but the release of both cAMP and PRL was stimulated in a dose- and time-dependent manner. These mutations apparently impaired the coupling between GnRH-R and **G proteins** involved in IP prodn., but not those involved in cAMP release. In M1 cells, Buserelin stimulation produced a significant increase in IP prodn., but neither cAMP nor PRL release was significantly stimulated. These findings are consistent with the previous suggestion that GnRH-stimulated PRL release is mediated by a cAMP second messenger system in transfected GGH3 cells.
IT 9002-62-4, Prolactin, biological studies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(LH-RH receptor Asn318 and Asp87,Asn318 mutations effect on receptor signal transduction and receptor regulation)

L11 ANSWER 19 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:549404 HCAPLUS
DOCUMENT NUMBER: 121:149404

TITLE: Evidence that signalling pathways by which thyrotropin-releasing hormone and gonadotropin-releasing hormone act are both common and distinct
AUTHOR(S): Kaiser, Ursula B.; Katzenellenbogen, Rachel A.; Conn, P. Michael; Chin, William W.
CORPORATE SOURCE: Div. Genetics., Dep. Med., Brigham Women's Hosp., Howard Hughes Med. Inst., Harvard Med. Sch., Boston, MA, 02115, USA
SOURCE: Mol. Endocrinol. (1994), 8(8), 1038-48
CODEN: MOENEN; ISSN: 0888-8809
DOCUMENT TYPE: Journal
LANGUAGE: English

AB TRH and GnRH receptors are each coupled to **G proteins** of the Gq/11 family. Activation of each of these receptors by their resp. **ligands** results in the stimulation of phospholipase C activity, leading to calcium mobilization and **protein** kinase C activation. Thus, the effects of TRH and GnRH may be mediated through the same intracellular signal transduction pathway. To compare responses to TRH and GnRH directly within one cell type, the authors have stably transfected the rat pituitary GH3 lactotroph cell line, which expresses the endogenous TRH receptor, with an expression vector contg. rat GnRH receptor cDNA. Transfected cells specifically bound GnRH with high affinity and responded to GnRH stimulation with an increase in PRL mRNA levels, analogous to their response to TRH stimulation. Stably transfected GH3 cells, which were then transiently transfected with luciferase reporter constructs contg. either the PRL or the glycoprotein hormone .alpha.-subunit promoter, responded to either GnRH or TRH stimulation with an increase in luciferase activity in a time- and dose-dependent fashion. The stimulatory effects of maximally effective concns. of TRH and GnRH were additive on PRL, but not .alpha.-subunit, gene expression. These data, coupled with evidence of cross-desensitization of .alpha.-subunit, but not PRL, promoter activity stimulation by TRH and GnRH, suggest that there may be differences in the signal transduction pathways activated by TRH and GnRH receptors in the regulation of PRL and .alpha.-subunit gene expression.

IT **9002-62-4, Prolactin**, biological studies
RL: BIOL (Biological study)
(gene for, transcription of, LH-RH and TRH stimulation of)

L11 ANSWER 20 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:156052 HCAPLUS
DOCUMENT NUMBER: 112:156052
TITLE: Structural differences between dopamine D2 receptors present in a rat pituitary adenoma and in transplantable rat pituitary tumors 7315a and MtTW15
AUTHOR(S): Bouvier, C.; Lagace, G.; Potier, M.; Collu, R.
CORPORATE SOURCE: Div. Med. Genet., Hop. Sainte-Justine, Montreal, PQ, Can.
SOURCE: J. Neurochem. (1990), 54(3), 815-22
CODEN: JONRA9; ISSN: 0022-3042
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The present study investigated the structure of dopamine (DA) D2 receptors present in an estrone-induced, **prolactin** (PRL)-secreting, DA-sensitive adenoma and in two PRL-secreting and DA-insensitive transplantable tumors 7315a and MtTW15, in order to identify better the anomalies present in DA-resistant lactotrophs. D2 receptors were found in both a high- and a low-affinity state in adenomatous lactotrophs as shown by displacement studies with the agonist N-propyl-norapomorphine (NPA),

but only in the low-affinity state in the two DA-resistant tumors. Treatment with the alkylating agent N-ethylmaleimide induced a disappearance of the high-affinity state of the D2 receptor in the adenoma and a redn. in receptor concn., but did not have any effect on the affinity of receptors present in DA-resistant tumors. Moreover, target size anal. and radiation inactivation studies of D2 receptors, using membranes preincubated with NPA and [3H]spiperone as **ligand** or using [3H]NPA as **ligand** on membranes prepns., have shown the presence of distinct structural differences between adenomatous and tumoral D2 receptors and between the two tumoral receptors themselves; these results suggest that the normal function unit of the D2 receptor is a dimer assocd. with a guanine nucleotide-binding **protein** (**G protein**) subunit and that tumoral D2 receptors may exist in various polymeric forms unassocd. with **G proteins**. The anomalies found to be present in tumoral D2 receptor complexes may be responsible for the insensitivity of these tumors to dopaminergic agonists' inhibitory activity on PRL release and tumor growth.

IT **9002-62-4, Prolactin**, biological studies
RL: BIOL (Biological study)
(secretion of, by **prolactinomas**, dopamine-resistant, dopamine D2 receptor structure in relation to)

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DICTIONARY FILE UPDATES: 31 MAR 2002 HIGHEST RN 403640-18-6

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http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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1	RN	383450-37-1	REGISTRY
2	RN	383450-36-0	REGISTRY
3	RN	383450-35-9	REGISTRY
4	RN	383450-34-8	REGISTRY
5	RN	383450-33-7	REGISTRY
6	RN	383450-32-6	REGISTRY
7	RN	383450-31-5	REGISTRY
8	RN	383450-30-4	REGISTRY
9	RN	383450-29-1	REGISTRY
10	RN	383450-28-0	REGISTRY
11	RN	383450-27-9	REGISTRY
12	RN	383450-26-8	REGISTRY
13	RN	383450-25-7	REGISTRY
14	RN	383450-24-6	REGISTRY
15	RN	383450-23-5	REGISTRY
16	RN	383450-22-4	REGISTRY
17	RN	383450-21-3	REGISTRY
18	RN	383450-20-2	REGISTRY
19	RN	383450-19-9	REGISTRY
20	RN	383450-18-8	REGISTRY
21	RN	383450-17-7	REGISTRY
22	RN	383450-16-6	REGISTRY
23	RN	383450-15-5	REGISTRY
24	RN	383450-14-4	REGISTRY
25	RN	383450-13-3	REGISTRY
26	RN	383450-12-2	REGISTRY
27	RN	383450-11-1	REGISTRY
28	RN	383450-10-0	REGISTRY
29	RN	383450-09-7	REGISTRY
30	RN	383450-08-6	REGISTRY
31	RN	383450-07-5	REGISTRY
32	RN	383450-06-4	REGISTRY
33	RN	383450-05-3	REGISTRY
34	RN	383449-51-2	REGISTRY
35	RN	271564-86-4	REGISTRY
36	RN	271564-84-2	REGISTRY
37	RN	271564-83-1	REGISTRY
38	RN	271564-81-9	REGISTRY
39	RN	271564-80-8	REGISTRY
40	RN	271564-79-5	REGISTRY
41	RN	271564-78-4	REGISTRY
42	RN	271564-77-3	REGISTRY

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43          RN   271564-76-2  REGISTRY
44          RN   271564-75-1  REGISTRY
45          RN   271564-74-0  REGISTRY
46          RN   271564-73-9  REGISTRY
47          RN   271564-72-8  REGISTRY
48          RN   263096-44-2  REGISTRY
49          RN   211485-95-9  REGISTRY
50          RN   211485-84-6  REGISTRY
51          RN   197665-29-5  REGISTRY
52          RN   197665-28-4  REGISTRY
53          RN   197665-27-3  REGISTRY
54          RN   197665-26-2  REGISTRY
55          RN    39362-14-6  REGISTRY
DR   9047-45-4
56          RN     9035-54-5  REGISTRY
DR   104521-44-0
57          RN     9002-62-4  REGISTRY


=> d ide can 1 5 10 15 20 25 30 34 35 40 48 49 51 55 56 57

L12  ANSWER 1 OF 57  REGISTRY  COPYRIGHT 2002 ACS
RN   383450-37-1  REGISTRY
CN   DNA (human G protein coupled receptor GPR8 ligand-specifying 51-nucleotide
     fragment) (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   126: PN: WO0198494 SEQID: 125 claimed DNA
FS   NUCLEIC ACID SEQUENCE
MF   Unspecified
CI   MAN
SR   CA
LC   STN Files:   CA, CAPLUS

*** STRUCTURE DIAGRAM IS NOT AVAILA8LE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
               1 REFERENCES IN FILE CA (1967 TO DATE)
               1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE   1:  136:65196

L12  ANSWER 5 OF 57  REGISTRY  COPYRIGHT 2002 ACS
RN   383450-33-7  REGISTRY
CN   DNA (human G protein coupled receptor GPR8 ligand-specifying 51-nucleotide
     fragment) (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   120: PN: WO0198494 SEQID: 119 claimed DNA
FS   NUCLEIC ACID SEQUENCE
MF   Unspecified
CI   MAN
SR   CA
LC   STN Files:   CA, CAPLUS

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
               1 REFERENCES IN FILE CA (1967 TO DATE)
               1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE   1:  136:65196
```

L12 ANSWER 10 OF 57 REGISTRY COPYRIGHT 2002 ACS
RN **383450-28-0** REGISTRY
CN DNA (human G protein coupled receptor GPR8 ligand-specifying 66-nucleotide fragment) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 115: PN: WO0198494 SEQID: 114 claimed DNA
FS NUCLEIC ACID SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS

*** STRUCTURE DIAGRAM IS NOT AVAILA8LE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:65196

L12 ANSWER 15 OF 57 REGISTRY COPYRIGHT 2002 ACS
RN **383450-23-5** REGISTRY
CN DNA (swine G protein coupled receptor GPR8 ligand-specifying 90-nucleotide fragment) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 76: PN: WO0198494 SEQID: 76 claimed DNA
FS NUCLEIC ACID SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS

*** STRUCTURE DIAGRAM IS NOT AVAILA8LE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:65196

L12 ANSWER 20 OF 57 REGISTRY COPYRIGHT 2002 ACS
RN **383450-18-8** REGISTRY
CN DNA (swine G protein coupled receptor GPR8 ligand-specifying 69-nucleotide fragment) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 58: PN: WO0198494 SEQID: 58 claimed DNA
FS NUCLEIC ACID SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS

*** STRUCTURE DIAGRAM IS NOT AVAILA8LE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:65196

L12 ANSWER 25 OF 57 REGISTRY COPYRIGHT 2002 ACS
RN **383450-13-3** REGISTRY

CN DNA (human G protein coupled receptor GPR8 ligand-specifying 72-nucleotide fragment) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 31: PN: WO0198494 SEQID: 31 claimed DNA
FS NUCLEIC ACID SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:65196

L12 ANSWER 30 OF 57 REGISTRY COPYRIGHT 2002 ACS
RN **383450-08-6** REGISTRY
CN DNA (human G protein coupled receptor GPR8 ligand-specifying 87-nucleotide fragment) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 26: PN: WO0198494 SEQID: 26 claimed DNA
FS NUCLEIC ACID SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:65196

L12 ANSWER 34 OF 57 REGISTRY COPYRIGHT 2002 ACS
RN **383449-51-2** REGISTRY
CN DNA (human G protein coupled receptor GPR8 125-amino acid ligand cDNA) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 14: PN: WO0198494 SEQID: 14 claimed DNA
FS NUCLEIC ACID SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:65196

L12 ANSWER 35 OF 57 REGISTRY COPYRIGHT 2002 ACS
RN **271564-86-4** REGISTRY
CN G protein-coupled receptor (rat 203-amino acid) (9CI) (CA INDEX NAME)
OTHER NAMES:

CN 47: PN: WO0029441 SEQID: 50 claimed protein
CN 50: PN: WO0166134 SEQID: 50 claimed protein
CN Protein (rat clone WO-01/66134A1 prolactin secretion-modulating polypeptide 203-amino acid isoform)
CN RFamide-related peptide, prepro- (Rattus norvegicus)
CN RFRP, prepro- (Rattus norvegicus)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
3 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:236443

REFERENCE 2: 134:25483

REFERENCE 3: 133:16312

L12 ANSWER 40 OF 57 REGISTRY COPYRIGHT 2002 ACS
RN **271564-79-5** REGISTRY
CN DNA (rat G protein-coupled receptor 203-amino acid gene) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 19: PN: WO0029441 SEQID: 19 claimed DNA
CN 19: PN: WO0166134 SEQID: 19 claimed DNA
CN DNA (rat prolactin secretion-modulating polypeptide 203-amino acid isoform cDNA)
FS NUCLEIC ACID SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:236443

REFERENCE 2: 133:16312

L12 ANSWER 48 OF 57 REGISTRY COPYRIGHT 2002 ACS
RN **263096-44-2** REGISTRY
CN Neuropeptide FF receptor (human clone pcDNA3.1-hNPFF1 subtype 1) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 51: PN: WO0029441 SEQID: 54 claimed protein
CN 54: PN: WO0166134 SEQID: 54 claimed protein
CN 6: PN: WO0018438 SEQID: 8 claimed protein
CN 8: PN: US6262246 SEQID: 8 claimed protein
CN G protein-coupled receptor (human 430-amino acid)
CN GenBank AF268898-derived protein GI 11907913
CN Neuropeptide FF receptor 1 (human)

CN Neuropeptide FF receptor hNPFF1 (human pcDNA3.1-hNPFF1)
CN NPFF1 (human)
CN Protein (human clone WO-01/66134A1 prolactin secretion-modulating polypeptide 430-amino acid isoform)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
6 REFERENCES IN FILE CA (1967 TO DATE)
6 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:236443

REFERENCE 2: 135:117950

REFERENCE 3: 134:157852

REFERENCE 4: 134:25483

REFERENCE 5: 133:16312

REFERENCE 6: 132:261389

L12 ANSWER 49 OF 57 REGISTRY COPYRIGHT 2002 ACS
RN **211485-95-9** REGISTRY
CN Prolactin (cattle signal peptide) fusion protein with synthetic octapeptide (FLAG epitope) fusion protein with 7-69-thrombin receptor [7-leucyl,8-asparty1,15-.alpha. amino acid,16-.alpha. amino acid,17-.alpha. amino acid,18-.alpha. amino acid,19-.alpha. amino acid] (human HEL cell reduced) fusion protein with 147-474-calcitonin receptor (human isoform reduced) (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:171503

L12 ANSWER 51 OF 57 REGISTRY COPYRIGHT 2002 ACS
RN **197665-29-5** REGISTRY
CN Protein (human prolactin signal peptide fusion protein with human .kappa.-receptor OR1) (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 127:314833

L12 ANSWER 55 OF 57 REGISTRY COPYRIGHT 2002 ACS
RN **39362-14-6** REGISTRY
CN Prolactin-releasing factor (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Lactogenic hormone-releasing factor
CN Prolactin-releasing hormone
CN Prolactin-releasing peptide
CN Prolactoliberin
DR 9047-45-4
MF Unspecified
CI PMS, MAN
PCT Manual registration
LC STN Files: AGRICOLA, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CAPLUS, CIN, DDFU, DRUGU, EMBASE, TOXCENTER, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
149 REFERENCES IN FILE CA (1967 TO DATE)
149 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:210832

REFERENCE 2: 136:210667

REFERENCE 3: 136:197676

REFERENCE 4: 136:194483

REFERENCE 5: 136:112833

REFERENCE 6: 136:80305

REFERENCE 7: 136:64184

REFERENCE 8: 136:876

REFERENCE 9: 135:362582

REFERENCE 10: 135:352919

L12 ANSWER 56 OF 57 REGISTRY COPYRIGHT 2002 ACS
RN **9035-54-5** REGISTRY
CN Lactogen, placental (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Choriomammotropin
CN Chorionic growth hormone-prolactin
CN Chorionic mammotropin
CN Chorionic somatomammotropin
CN Lactogenic hormone, placental
CN Lactosomatic hormone
CN Lactosomatotropic hormone
CN Placental lactogen
CN Placental lactogen II
CN Placental lactogen-2

CN Placental lactogenic hormone
CN Somatomammotrophin
CN Somatomammotropic hormone
CN Somatomammotropin
DR 104521-44-0
MF Unspecified
CI PMS, MAN
PCT Manual registration
LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CHEMCATS, CSCHEM, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, MEDLINE, PROMT, TOXCENTER, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
1991 REFERENCES IN FILE CA (1967 TO DATE)
37 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1993 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:132992

REFERENCE 2: 136:100074

REFERENCE 3: 136:97261

REFERENCE 4: 136:66588

REFERENCE 5: 136:51990

REFERENCE 6: 136:31806

REFERENCE 7: 136:2090

REFERENCE 8: 136:1495

REFERENCE 9: 136:1073

REFERENCE 10: 136:843

L12 ANSWER 57 OF 57 REGISTRY COPYRIGHT 2002 ACS
RN **9002-62-4** REGISTRY
CN Prolactin (8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN Adenohypophyseal luteotropin
CN Anterior pituitary luteotropin
CN Bovine lactogenic hormone
CN Galactin
CN Lactin
CN Lactogen, pituitary
CN Lactogenic hormone
CN Lactosomatotropic hormone
CN Lactosomatotropin
CN Luteotrophin
CN Luteotropic hormone
CN Luteotropic hormone LTH
CN Luteotropin
CN Mammotropin
CN Paralactin
CN Pituitary lactogenic hormone
CN PRL
MF Unspecified

```
CI    PMS, COM, MAN
PCT   Manual registration
LC    STN Files:   ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO,
        CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CIN, CSCHEM,
        CSNB, DDFU, DIOGENES, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA,
        MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PIRA, PROMT, RTECS*,
        TOXCENTER, USPATFULL
          (*File contains numerically searchable property data)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
           24963 REFERENCES IN FILE CA (1967 TO DATE)
             178 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
           24972 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE   1:  136:215666

REFERENCE   2:  136:215200

REFERENCE   3:  136:214990

REFERENCE   4:  136:214905

REFERENCE   5:  136:214822

REFERENCE   6:  136:214753

REFERENCE   7:  136:211040

REFERENCE   8:  136:210885

REFERENCE   9:  136:210833

REFERENCE  10:  136:210832


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L1            32 SEA FILE=REGISTRY ABB=ON  PLU=ON  TPDINPAWYXXRGIRPVGRFXX|SRAHQH
                 SMEIRTPDINPAWYAGRGIRPVGRF|TPDINPAWYAGRGIRPVGRF|SRAHQHSMETRTPDIN
                 PAWYTGRGIRPVGRF|TPDINPAWYTGRGIRPVGRF|SRTHRHSMEIRTPDINPAWYASRGIR
                 PVGRF|TPDINPAWYASRGIRPVGRF/SQSP
L2            25 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L1
L3            85 SEA FILE=REGISTRY ABB=ON  PLU=ON  G-PROTEIN?/CN
L4          1103 SEA FILE=REGISTRY ABB=ON  PLU=ON  LIGAND(L)(POLYPEPTIDE OR
                 PEPTIDE OR PROTEIN)
L5           584 SEA FILE=REGISTRY ABB=ON  PLU=ON  PROLACTIN/BI
L6         43103 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3 OR G(W)PROTEIN?
L7         56928 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L4 OR LIGAND(L)(POLYPEPTIDE
                 OR PEPTIDE OR PROTEIN)
L8         67365 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L5 OR ?PROLACT?
L9          3473 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L6(L)L7
L10           28 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9 AND L8
L11           20 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L10 NOT L2
L13          319 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9 AND (?VARIANIS? OR
                 ?GONECYSTCACOG? OR ?MENOPAUS? OR ?THYROID? OR ?METABOLIS? OR
                 ?ADENOMATOS? OR ?TUMOR? OR ?EMMENIOPATH? OR ?AUTOIMM? OR
                 ?PROLACTINOM? OR ?INFERTIL? OR ?IMPOTENCE? OR ?AMENORRH? OR
                 ?GALACTORR? OR ?ACROMEGA? OR ?CHIARI? OR ?FROMMEL? OR ?ARGONZ?
                 OR ?CASTILO? OR ?FORBES?)
L14          239 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L13 AND (?MODULAT? OR
```

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                REGULAT? OR INHIBIT? OR  STIMUL?)
L15          69 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L14 AND (?MEDICIN? OR ?DRUG?
                OR ?THERAP? OR ?PHARM?)
L16          68 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L15 NOT (L1 OR L11)
L19        7462 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L6(W)COUPLED(W)RECEPTOR
L20          48 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L19 AND L16


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=> d ibib abs hitrn l20 1-48

L20  ANSWER 1 OF 48  HCAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         2002:204500  HCAPLUS
TITLE:                    Guanosine phosphate binding protein coupled receptors
                          in prostate cancer: A review
AUTHOR(S):                Raj, Ganesh V.; Barki-Harrington, Liza; Kue, Pao F.;
                          Daaka, Yehia
CORPORATE SOURCE:         Departments of Surgery and Pharmacology-Cancer
                          Biology, Duke University Medical Center, Durham, NC,
                          27710, USA
SOURCE:                   Journal of Urology (Hagerstown, MD, United States)
                          (2002), 167(3), 1458-1463
                          CODEN: JOURAA; ISSN: 0022-5347
PUBLISHER:                Lippincott Williams & Wilkins
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   Androgens are the primary growth promoters of the prostate gland and yet
     prostate tumors progress despite androgen ablation.  This
     progression suggests a role for addnl. cellular factors in the progression
     to androgen independent disease.  We examd. the role of a family of
     extracellular signal regulators, namely the guanosine phosphate
     binding (G) protein coupled receptor
     (GPCR) family, in prostate cancer.  A comprehensive review of the
     literature was performed on GPCRs and prostate cancer, and supplemented
     with published and unpublished observations made at our lab.  Emphasis was
     placed on the mechanistic aspects of mitogenic signaling pathways involved
     to identify potential targets for therapy.  Expression of some
     GPCRs and GPCR ligands is elevated in prostate cancer cells and
     adjacent prostatic stromal tissue.  In vitro studies demonstrate that
     activation of GPCRs confers a distinct growth and survival advantage on
     prostate cancer cells, including enhanced proliferation and decreased
     programmed cell death (apoptosis).  Specifically stimulation of
     GPCRs for lysophosphatidic acid and bradykinin induces proliferation of
     androgen independent prostate cancer cells via the activation of the
     extracellular signal regulated kinase (ERK) pathway.  Induction
     of ERK by the bradykinin and lysophosphatidic acid in prostate cells
     proceeds via distinct pathways and involves G.alpha.q and G.beta..gamma.
     subunits, resp.  The G.beta..gamma. dependent activation of ERK requires
     tyrosine kinases, including epidermal growth factor receptor and c-Src.
     Furthermore, stimulation with LPA enhances the survival of
     prostate cancer cells via activation of the inducible transcription factor
     nuclear factor-.kappa.B.  GPCR stimulation induces proliferation
     and prevents apoptosis of hormone independent prostate cancer cells,
     indicating their important role in the progression of prostate cancer.
     While further confirmatory studies are required to verify the role of
     GPCRs in disease progression, the therapeutic implications of
     these studies may enhance the armamentarium in the fight against prostate
     cancer.
```

L20 ANSWER 2 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:190254 HCAPLUS
TITLE: Neurokinin receptor **pharmacology** and function
AUTHOR(S): Lachowicz, Jean E.
CORPORATE SOURCE: Department of CNS and Cardiovascular Research, Schering-Plough Research Institute, Kenilworth, NJ, 07033, USA
SOURCE: Abstracts of Papers, 223rd ACS National Meeting, Orlando, FL, United States, April 7-11, 2002 (2002), MEDI-135. American Chemical Society: Washington, D. C.
CODEN: 69CKQP
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB The neurokinin receptors, NK1, NK2, and NK3 belong to the G-**protein coupled receptor** family. Tachykinins, the endogenous **ligands** of these receptors, share a common C-terminal amino acid sequence. The most widely characterized tachykinins, substance P, neurokinin A, and neurokinin B, arise from the preprotachykinin A and B genes and bind with highest affinity to NK1, NK2, and NK3 receptors, resp. Tachykinins and their receptors are distributed widely throughout the CNS and periphery, where they are involved in smooth muscle contraction, neurotransmitter **modulation**, hormone secretion, inflammation, respiratory control, nociception, and response to stress. Evidence collected from clin. trials as well as studies of genetically altered mice and other animal models has suggested that neurokinin receptor **ligands** may be effective in treating emesis, depression, anxiety, visceral pain, rheumatoid arthritis, **tumor** proliferation, infection, asthma, and other disorders. Characterization of novel tachykinins may shed more light on the mechanisms by which neurokinin receptors influence physiol. functions.

L20 ANSWER 3 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:140716 HCAPLUS
TITLE: Thrombin **regulation** of cell function through protease-activated receptors: implications for **therapeutic** intervention
AUTHOR(S): Derian, C. K.; Damiano, B. P.; D'Andrea, M. R.; Andrade-Gordon, P.
CORPORATE SOURCE: The R. W. Johnson Pharmaceutical Research Institute, Spring House, PA, 19477-0776, USA
SOURCE: Biochemistry (Moscow, Russian Federation)(Translation of Biokhimiya (Moscow, Russian Federation)) (2002), 67(1), 56-64
CODEN: BIORAK; ISSN: 0006-2979
PUBLISHER: MAIK Nauka/Interperiodica Publishing
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The serine protease thrombin is well recognized as being pivotal to the maintenance of hemostasis under both normal and pathol. conditions. Its cellular actions are mediated through a unique family of protease-activated receptors (PARs). These receptors represent a novel family of **G protein-coupled receptors** that undergo proteolytic cleavage of their amino terminus and subsequent autoactivation by a tethered **peptide ligand**. This paper reviews the consequences of PAR activation in thrombosis, vascular injury, inflammation, tissue injury, and within the

tumor microenvironment.
REFERENCE COUNT: 125 THERE ARE 125 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 4 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:51533 HCAPLUS
DOCUMENT NUMBER: 136:117381
TITLE: Bifunctional antibody fusion proteins for targeted gene delivery
INVENTOR(S): Nemerow, Glen R.; Li, Erguang
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.; The Scripps Research Institute
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002004522	A2	20020117	WO 2001-EP7878	20010709

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-613017 A 20000710
AB The authors disclose methods and products for targeting delivery vectors, such as adenoviral gene delivery particles, to selected cell types. The targeting is effected by a bifunctional mol. that specifically complexes with (1) a protein on the vector particle surface and (2) a cell surface proteins. In one example, the authors demonstrate improved adenovirus vector binding, internalization, and transgene gene expression in targeted melanoma cells using a fusion protein of **tumor** necrosis factor-.alpha. and an anti-penton base monoclonal antibody. Virus internalization and reporter gene expression was dependent on activation of phosphatidylinositol 3' kinase via the **tumor** necrosis factor receptor signaling pathway.

L20 ANSWER 5 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:43366 HCAPLUS
DOCUMENT NUMBER: 136:215187
TITLE: Role of tyrosine phosphorylation in ligand-independent sequestration of CXCR4 in human primary monocytes-macrophages
AUTHOR(S): Wang, Jinhai; Guan, Ennan; Roderiquez, Gregory; Calvert, Valerie; Alvarez, Raymond; Norcross, Michael A.
CORPORATE SOURCE: Laboratory of Gene Regulation, Division of Therapeutic Proteins, Center for Biologics Evaluation and Research, Food and Drug Administration, Bethesda, MD, 20892, USA

SOURCE: Journal of Biological Chemistry (2001), 276(52), 49236-49243
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The chemokine stromal cell-derived factor (SDF)-1 and its receptor, CXCR4, play important roles in human immunodeficiency virus type 1 (HIV-1) pathophysiol., leukocyte trafficking, inflammation, hematopoiesis, embryogenesis, angiogenesis, and cancer metastasis. The effects of cytokines on the **regulation** of CXCR4 function were investigated in human primary monocytes-macrophages. The expression of functional CXCR4 on the cell surface was demonstrated by the detection of **ligand**-induced Ca2+ mobilization, chemotaxis, and **ligand** -induced receptor endocytosis. Surface CXCR4 expression was down-**regulated** by cytokines interleukin-4 (IL-4), IL-13, and granulocyte-macrophage colony-**stimulating** factor (GM-CSF) and up-**regulated** by IL-10 and transforming growth factor-.beta.1. Down-**regulation** was mediated post-translationally, in the absence of **protein** degrdn., through an endocytotic mechanism. In contrast to SDF-1.alpha.-induced CXCR4 endocytosis, cytokine-induced endocytosis of this receptor was independent of actin filament polymn. GM-CSF increased the expression of G **protein-coupled receptor** kinase 3 (GRK3), -arrestin-1, Pyk2, and focal adhesion kinase (FAK). Cytokine treatment also increased the total and tyrosine-specific phosphorylation of CXCR4 as well as the phosphorylation of FAK on tyrosine 397. It also induced the formation of GRK3-CXCR4 or FAK-CXCR4 complexes. Infection of macrophages by primary R5X4 and X4 isolates of HIV-1 was **inhibited** by IL-4, IL-13, and GM-CSF, an effect that was assocd. with down-**regulation** of surface CXCR4 expression. These data indicate that **ligand** -dependent and **ligand**-independent endocytoses of CXCR4 are mediated by different mechanisms. Cytokine-induced endocytosis of chemokine receptors may be of **therapeutic** value in HIV-1 infection, inflammation, **tumor** metastasis, and defective hematopoiesis.

REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 6 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:935632 HCAPLUS
DOCUMENT NUMBER: 136:64088
TITLE: A recombinant cell line expressing GPCRx11 as a functional receptor validated by angiopeptin and useful for screening of agonists and antagonists
INVENTOR(S): Lannoy, Vincent; Brezillon, Stephane; Detheux, Michel; Parmentier, Marc; Govarts, Cedric
PATENT ASSIGNEE(S): Euroscreen S.A., Belg.
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001098330	A2	20011227	WO 2001-BE104	20010620

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:
US 2000-212913P P 20000620
US 2000-217494P P 20000711
EP 2001-870015 A 20010126
EP 2001-870024 A 20010212

AB The present invention is related to a G-protein coupled receptor or GPCRx11 similar to rat RTA receptor (37) and expressed in testis, thymus and uterus. Aequorin cell line expressing GPCRx1I has been used for screening of tissue exts. and ref. ligands. GPCRx11 cells gave a specific signal with synthetic angiopeptin and a somatostatin analog allowing to validate this cell line for screening of natural or synthetic agonists and antagonists. In parallel, extended tissue distribution and polyclonal antibodies have been produced to facilitate GPCRx1I characterization.

L20 ANSWER 7 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:868494 HCAPLUS
DOCUMENT NUMBER: 136:32762
TITLE: Novel G protein-coupled receptor sequence homologs from human and uses in treatment and diagnosis of mental disorder thereof
INVENTOR(S): Vogeli, Gabriel
PATENT ASSIGNEE(S): Pharmacia + Upjohn Company, USA
SOURCE: PCT Int. Appl., 138 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001090149	A2	20011129	WO 2001-US16419	20010522

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:
US 2000-206138P P 20000522
US 2000-206139P P 20000522
US 2000-208976P P 20000602

AB The present invention provides a gene encoding a G protein-coupled receptor termed nGPCR-x (x from 2646 to 2687); constructs and recombinant host cells incorporating the genes; the nGPCR-x polypeptides encoded by the gene; antibodies to the nGPCR-x polypeptides; and methods of making and using all of the foregoing.

L20 ANSWER 8 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:798427 HCAPLUS
DOCUMENT NUMBER: 135:353806
TITLE: Human **G protein-coupled receptor**-like MOLX proteins and the nucleic acids that encode them
INVENTOR(S): Vernet, Corine A. M.; Fernandes, Elma R.; Gerlach, Valerie; Shimkets, Richard A.; Malyankar, Uriel M.; Boldog, Ferenc L.; Zerhusen, Bryan D.; Spytek, Kimberly A.; Majumder, Kumud; Tchernev, Velizar T.; Padigaru, Muralidhara; Patturajan, Meera; Burgess, Catherine E.; Gangolli, Esha A.; Smithson, Glennda; Rastelli, Luca; MacDougall, John R.; Taupier, Raymond J., Jr.; Grosse, William M.; Szekeres, Edward S., Jr.; Alsoborook, John P., II
PATENT ASSIGNEE(S): Curagen Corp., USA
SOURCE: PCT Int. Appl., 227 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001081578	A2	20011101	WO 2001-US13578	20010426

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 2000-200158P	P	20000426
US 2000-200780P	P	20000428
US 2000-201006P	P	20000501
US 2000-201007P	P	20000501
US 2000-201236P	P	20000501
US 2000-201238P	P	20000502
US 2000-201474P	P	20000503
US 2000-201508P	P	20000503
US 2000-220591P	P	20000725
US 2000-232678P	P	20000915
US 2001-263217P	P	20010122
US 2001-265160P	P	20010130

AB Disclosed herein are 15 nucleic acid sequences that encode human **G protein-coupled receptor**-related polypeptides, designated MOL1 to MOL10b. Also disclosed are polypeptides encoded by these nucleic acid sequences, and antibodies, which immunospecifically-bind to the polypeptide, as well as derivs., variants, mutants, or fragments of the aforementioned polypeptide, polynucleotide, or antibody. Nearest neighbor sequence homologies, protein domains, tissue expression profiles, and chromosomal location are also provided. The invention further discloses **therapeutic**, diagnostic and research methods for diagnosis, treatment, and prevention of disorders involving any one of these novel human nucleic acids and proteins.

L20 ANSWER 9 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:798425 HCAPLUS
DOCUMENT NUMBER: 135:340268
TITLE: A novel **G protein-coupled receptor** sequence homolog Con-218 from human and rat and uses in treatment and diagnosis of mental disorder thereof
INVENTOR(S): Lind, Peter; Berthold, Malin
PATENT ASSIGNEE(S): Pharmacia + Upjohn Company, USA
SOURCE: PCT Int. Appl., 126 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001081576	A2	20011101	WO 2001-US12690	20010419

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-198600P P 20000419
AB The present invention provides a gene encoding a **G protein-coupled receptor** termed Con-218; constructs and recombinant host cells incorporating the genes; the Con-218 polypeptides encoded by the gene; antibodies to the Con-218 polypeptides; and methods of making and using all of the foregoing.

L20 ANSWER 10 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:798286 HCAPLUS
DOCUMENT NUMBER: 135:340255
TITLE: A novel **G protein-coupled receptor** sequence homolog nGPCR-2644 from human and uses in treatment and diagnosis of mental disorder thereof
INVENTOR(S): Lind, Peter; Sejlitz, Torsten; Vogeli, Gabriel
PATENT ASSIGNEE(S): Pharmacia + Upjohn Company, USA
SOURCE: PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001081410	A2	20011101	WO 2001-US13249	20010425

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,

RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2000-199558P P 20000425
AB The present invention provides a gene encoding a **G protein-coupled receptor** termed nGPCR-2644; constructs and recombinant host cells incorporating the genes; the nGPCR-2644 polypeptides encoded by the gene; antibodies to the nGPCR-2644 polypeptides; and methods of making and using all of the foregoing.

L20 ANSWER 11 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:798283 HCAPLUS
DOCUMENT NUMBER: 135:340253
TITLE: A novel **G protein-coupled receptor** sequence homolog Con-235 from human and rat and uses in treatment and diagnosis of mental disorder thereof
INVENTOR(S): Lind, Peter; Vogeli, Gabriel; Wood, Linda S.; Merchant, Kalpana M.; Soderberg, Charlotte
PATENT ASSIGNEE(S): Pharmacia + Upjohn Company, USA
SOURCE: PCT Int. Appl., 128 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001081407	A2	20011101	WO 2001-US13053	20010424

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2000-199632P P 20000425
AB The present invention provides a gene encoding a G **protein-coupled receptor** termed Con-235; constructs and recombinant host cells incorporating the genes; the Con-235 polypeptides encoded by the gene; antibodies to the Con-235 polypeptides; and methods of making and using all of the foregoing.

L20 ANSWER 12 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:798254 HCAPLUS
DOCUMENT NUMBER: 135:353786
TITLE: Human **G protein-coupled receptor** proteins and the nucleic acids that encode them
INVENTOR(S): Padigaru, Muralidhara; Mishra, Vishnu; Spytek, Kimberly A.; Grosse, William M.; Szekeres, Edward S., Jr.; Alsobrook, John P., II; Burgess, Chaterine E.; Casman, Stacie J.; Lepley, Denise M.; Gangolli, Esha A.; MacDouglass, John R.; Smithson, Glennda

PATENT ASSIGNEE(S): Curagen Corp., USA
SOURCE: PCT Int. Appl., 243 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001081378	A2	20011101	WO 2001-US13680	20010427

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:
US 2000-199947P P 20000427
US 2000-199960P P 20000427
US 2000-275226P P 20000814
US 2000-256399P P 20001218
US 2000-256624P P 20001218
US 2000-258159P P 20001222
US 2000-258511P P 20001228
US 2000-258828P P 20001228
US 2000-259659P P 20010104

AB Disclosed herein are 28 nucleic acid sequences that encode human **G protein-coupled receptor**-related polypeptides. Also disclosed are polypeptides encoded by these nucleic acid sequences, and antibodies, which immunospecifically-bind to the polypeptide, as well as derivs., variants, mutants, or fragments of the aforementioned polypeptide, polynucleotide, or antibody. Nearest neighbor sequence homologies, protein domains, tissue expression profiles, and chromosomal location are also provided. The invention further discloses **therapeutic**, diagnostic and research methods for diagnosis, treatment, and prevention of disorders involving any one of these novel human nucleic acids and proteins.

L20 ANSWER 13 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:763063 HCAPLUS
DOCUMENT NUMBER: 135:314460
TITLE: A human **G protein-coupled receptor** identified by sequence homology and uses in treatment of mental disorder
INVENTOR(S): Vogeli, Gabriel; Lind, Peter; Sejlitz, Torsten; Berthold, Malin
PATENT ASSIGNEE(S): Pharmacia + Upjohn Company, USA
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2001077175 A2 20011018 WO 2001-US11331 20010406
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2000-195228P P 20000406
US 2000-251313P P 20001205

AB The present invention provides a gene encoding a **G protein-coupled receptor** termed nGPCR-2037; constructs and recombinant host cells incorporating the genes; the nGPCR-2037 polypeptides encoded by the gene; antibodies to the nGPCR-2037 polypeptides; and methods of making and using all of the foregoing.

L20 ANSWER 14 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:763060 HCAPLUS
DOCUMENT NUMBER: 135:299092
TITLE: Non-endogenous, constitutively activated known **G protein-coupled receptors** useful for **ligand** screening assays
INVENTOR(S): Lehmann-Bruinsma, Karin; Liaw, Chen W.; Lin, I-Lin
PATENT ASSIGNEE(S): Arena Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 396 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001077172	A2	20011018	WO 2001-US11098	20010405

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2000-195747P P 20000407

AB The invention disclosed in this patent document relates to transmembrane receptors, more particularly to a human **G protein-coupled receptor** (GPCR) for which the endogenous **ligand** is known, and most particularly to mutated (non-endogenous) versions of the known GPCRs. Site-specific mutation ti a lysine residue is based on an algorithmic approach and is preferred at the 16th amino acid within intracellular loop 3 (IL3) region which is a positional distance from a conserved proline residue located within the transmembrane membrane 6 (TM6) region, thereby increasing the functional second messenger activity. The mutated GPCR versions are used in screening assays for the direct identification of candidate compds. as inverse agonists, agonists, and partial agonists. A GPCR fusion **protein**

is intended to enhance the efficacy of **G protein** coupling with the non-endogenous GPCR, and is preferred for screening with a non-endogenous, constitutively activated GPCR because such an approach increases the signal that is most preferably utilized in such screening techniques. This is important in facilitating a significant "signal to noise" ratio. Receptor-based assays are also described: (1) CRE-Luc reporter and (2) 8XCre-Luc reporter assays for Gs-assocd. receptors; (3) AP1 reporter and (4) SRF-Luc receptor assays for Gq-assocd. receptors.

L20 ANSWER 15 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:714217 HCAPLUS
DOCUMENT NUMBER: 136:745
TITLE: P2 nucleotide receptors in osteoclasts
AUTHOR(S): Naemsch, Lin N.; Du, Xiaobing; Sims, Stephen M.; Dixon, S. Jeffrey
CORPORATE SOURCE: CIHR Group in Skeletal Development and Remodeling, Department of Physiology, Division of Oral Biology, School of Dentistry, Faculty of Medicine & Dentistry, The University of Western Ontario, London, ON, N6A 5C1, Can.
SOURCE: Drug Development Research (2001), 53(2/3), 130-139
CODEN: DDREDK; ISSN: 0272-4391
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with refs. Osteoclasts are large, multinucleated cells responsible for the resorption of bone and other mineralized tissues. Whereas low concns. of extracellular ATP **stimulate** osteoclast formation and resorptive activity, high concns. **inhibit** osteoclast formation. Cell surface receptors for nucleotides are classified into two families-P2X (**ligand**-gated channels nonselective for cations) and P2Y (**G-protein-coupled receptors** linked, in most cases, to release of Ca2+ from intracellular stores). Several subtypes of P2 receptors are expressed by mammalian osteoclasts. The P2X4 receptor has been identified at both **protein** and mRNA levels and ATP activates a nonselective cation current with properties similar to that mediated by the cloned P2X4 channel. The P2X2 receptor is also expressed; however, currents with properties of P2X2 have yet to be identified. Functional and expression studies also support the existence of the P2X7 receptor, which is activated by high concns. of ATP. Application of nucleotides to osteoclasts elicits transient elevation of cytosolic free Ca2+ concn. and activation of Ca2+-dependent K+ channels. Both these responses are mediated, at least in part, by release of Ca2+ from intracellular stores, consistent with the presence of functional P2Y receptors. Expression of P2Y1 and P2Y2 receptors has been demonstrated in mammalian osteoclasts. The presence of multiple subtypes of P2 receptors may account for the biphasic effects of extracellular nucleotides on osteoclast function. These receptors represent potential targets for the development of novel **therapeutics** to **inhibit** bone resorption in diseases such as rheumatoid arthritis, osteoporosis, **tumor**-induced osteolysis, and periodontitis.
REFERENCE COUNT: 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 16 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:713376 HCAPLUS
DOCUMENT NUMBER: 135:283216
TITLE: **Peptide** derivatives recognized as

ligands by G protein-coupled receptor protein

INVENTOR(S): Kitada, Chieko; Nishizawa, Naoki; Hinuma, Shuji; Hosoya, Masaki

PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., USA

SOURCE: PCT Int. Appl., 136 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001070769	A1	20010927	WO 2001-JP2278	20010322

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2000-87114 A 20000323
JP 2000-288891 A 20000919

AB A novel **peptide** deriv. recognized as a **ligand** by a **G protein-coupled receptor protein**. This **peptide** deriv. is usable in, for example: (1) developing a receptor-binding assay system and screening candidate compds. for **drugs** with the use of a recombinant receptor **protein** expression system; and (2) developing **drugs** such as central function controlling agents, circulatory function controlling agents, heart function controlling agents, immune function controlling agents, digestive function controlling agents, metabolic function controlling agents or reproductive function controlling agents. A **peptide** Arg-Arg-Gln-Arg-Pro-Arg-Leu-Ser-Ala-Arg-Gly-Pro-Met-Pro-Phe(Cl) was prepd. by solid phase synthesis, and tested for its **inhibitory** effect on forskolin-induced cAMP formation in CHO-A10 clone 6 cells.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 17 OF 48 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:711677 HCAPLUS

DOCUMENT NUMBER: 136:64048

TITLE: Calcilytic compounds: potent and selective Ca2+ receptor antagonists that **stimulate** secretion of **parathyroid** hormone

AUTHOR(S): Nemeth, Edward F.; Delmar, Eric G.; Heaton, William L.; Miller, Michael A.; Lambert, Lyssa D.; Conklin, Rebecca L.; Gowen, Maxine; Gleason, John G.; Bhatnagar, Pradip K.; Fox, John

CORPORATE SOURCE: NPS Pharmaceuticals, Inc., Salt Lake City, UT, USA

SOURCE: Journal of Pharmacology and Experimental Therapeutics (2001), 299(1), 323-331
CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal
LANGUAGE: English
AB Despite the discovery of many ions and mols. that activate the Ca2+ receptor, there are no known ligands that block this receptor. Reported here are the **pharmacodynamic** properties of a small mol., NPS 2143, which acts as an antagonist at the Ca2+ receptor. This compd. blocked (IC50 of 43 nM) increases in cytoplasmic Ca2+ concns. [Ca2+]i elicited by activating the Ca2+ receptor in HEK 293 cells expressing the human Ca2+ receptor. NPS 2143, even when tested at much higher concns. (3 .mu.M), did not affect the activity of a no. of other **G protein-coupled receptors,** including those most structurally homologous to the Ca2+ receptor. NPS 2143 **stimulated parathyroid** hormone (PTH) secretion from bovine **parathyroid** cells (EC50 of 41 nM) over a range of extracellular Ca2+ concns. and reversed the effects of the calcimimetic compd. NPS R-467 on [Ca2+]i and on secretion of PTH. When infused i.v. in normal rats, NPS 2143 caused a rapid and large increase in plasma levels of PTH. Ca2+ receptor antagonists are termed calcilytics and NPS 2143 is the first substance (either at. or mol.) shown to possess such activity. The **pharmacodynamic** properties of NPS 2143 together with the recently demonstrated effects of this compd. on bone formation support the view that orally active calcilytic compds. might provide a novel anabolic **therapy** for osteoporosis.
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 18 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:693370 HCAPLUS
DOCUMENT NUMBER: 135:267689
TITLE: Human neuropeptide Y-like **G protein -coupled receptors,** polynucleotides encoding them and use in screening for **therapeutic** agents that modify NPY-GPCR
INVENTOR(S): Ramakrishnan, Shyam
PATENT ASSIGNEE(S): Bayer Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001068699	A2	20010920	WO 2001-EP2846	20010314

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-189877P P 20000316
US 2000-210743P P 20000612

AB The invention provides human neuropeptide Y-like **G protein-coupled receptor polypeptides** (and polynucleotides encoding them) which can be used to identify test

compds. which may act as agonists or antagonists at the receptor site. Human neuropeptide Y-like G **protein-coupled receptor** and fragments thereof are also useful in raising specific antibodies which can block the receptor and effectively prevent **ligand** binding. Reagents which **regulate** human neuropeptide Y **G protein-coupled receptor** (NPY-GPCR) **protein** and reagents which bind to human NPY-GPCR gene products can play a role in preventing, ameliorating, or correcting dysfunctions or diseases including, but not limited to, obesity, diabetes, anxiety, hypertension, cocaine withdrawal, congestive heart failure, memory enhancement, cardiac and cerebral vasospasm, pheochromocytoma, ganglioneuroblastoma, Huntington's disease, Alzheimer's disease, and Parkinson's disease. **Pharmaceutical** compns. contg. a NPY-GPCR **modulator** are also claimed.

L20 ANSWER 19 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:507951 HCAPLUS
DOCUMENT NUMBER: 135:87148
TITLE: Metal ion binding site-based method of identifying ligands of biological target molecules for **drug** discovery
INVENTOR(S): Elling, Christian E.; Gerlach, Lars Ole; Holst Lange, Birgitte; Pedersen, Jan Torleif; Schwartz, Thue W.
PATENT ASSIGNEE(S): 7TM Pharma, Den.
SOURCE: PCT Int. Appl., 114 pp.
COOEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001050127	A2	20010712	WO 2000-EP13389	20001229
WO 2001050127	A3	20020131		

W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TO, TG

PRIORITY APPLN. INFO.:

DK 1999-1879	A	19991230
OK 1999-1880	A	19991230
US 2000-175401P	P	20000111
US 2000-175994P	P	20000111
DK 2000-705	A	20000428
US 2000-202990P	P	20000509

OTHER SOURCE(S): MARPAT 135:87148
AB The invention provides a mol. approach for rapidly and selectively identifying small org. mol. **ligands**, i.e. compds., that are capable of interacting with and binding to specific sites on biol. target mols. The methods of the invention are applicable to any biol. target mol. that has or can be manipulated to have a metal-ion binding site. Biol. target mols. are e.g. **proteins**, **polypeptides**, oligopeptides, nucleic acids, carbohydrates,

nucleoproteins, glycoproteins, glycolipids, lipoproteins and derivs. thereof. More specifically, the biol. target mols. include membrane receptors, signal transduction **proteins**, scaffolding **proteins**, nuclear receptors, steroid receptors, intracellular receptors, transcription factors, enzymes, allosteric enzyme **regulatory proteins**, growth factors, hormones, neuropeptides and Igs. A very interesting group of biol. target mols. are membrane **proteins** such as, e.g., transmembrane **protein** (e.g. 7 TMs). The methods described herein make it possible to construct and screen libraries of compds. specifically directed against predetd. epitopes on the biol. target mols. The compds. are initially constructed to be bifunctional, i.e. having both a metal-ion binding moiety, which conveys them with the ability to bind to either a natural or an artificially constructed metal-ion binding site as well as a variable moiety, which is varied chem. to probe for interactions with specific parts of the biol. target mol. located spatially adjacent to the metal-ion binding site. Compds. may subsequently be further modified to bind to the unmodified biol. target mol. without help of the bridging metal-ion. The methods according to the invention may be performed easily and quickly and lead to unambiguous results. The compds. identified by the methods may themselves be employed for various applications or may be further derivatized or modified to provide novel compds. The methodol. of the invention is useful in **drug** discovery.

L20 ANSWER 20 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:489484 HCAPLUS
DOCUMENT NUMBER: 135:103349
TITLE: cDNA and protein sequences of novel human G **protein-coupled receptor** homologs nGPCR-x and their uses in **drug** screening and diagnosis of mental disorders
INVENTOR(S): Lind, Peter; Parodi, Luis A.; Lindberg, Eleni; Vogeli, Gabriel; Wood, Linda Susan; Hiebsch, Ronald R.; Ruff, Valerie
PATENT ASSIGNEE(S): Pharmacia + Upjohn Company, USA
SOURCE: PCT Int. Appl., 174 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001048015	A2	20010705	WO 2000-US35456	20001228

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:
US 1999-173339P P 19991228
US 2000-184305P P 20000223
US 2000-188880P P 20000313
US 2000-200534P P 20000427
US 2000-219492P P 20000720

US 2000-224321P P 20000811
US 2000-239062P P 20001009

AB The present invention provides a gene encoding a G **protein-coupled receptor** termed nGPCR-x; constructs and recombinant host cells incorporating the genes; the nGPCR-x polypeptides encoded by the gene; antibodies to the nGPCR-x polypeptides; and methods of making and using all of the foregoing. Novel G **protein-coupled receptors** (GPCRs) that may be of use in the diagnosis or treatment of disease are identified by sequence homol. Candidate sequences were identified by BLAST querying a proprietary DNA sequence database for GPCR-like sequences. Candidate sequences were cloned and sequenced.

L20 ANSWER 21 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:440314 HCAPLUS
DOCUMENT NUMBER: 135:300125
TITLE: Metastasis suppressor gene KiSS-1 encodes **peptide ligand** of a G-**protein-coupled receptor**
AUTHOR(S): Ohtaki, Tetsuya; Shintani, Yasushi; Honda, Susumu; Matsumoto, Hirokazu; Hori, Akiura; Kanehashi, Kimiko; Terao, Yasuko; Kumano, Satoshi; Takatsu, Yoshihiro; Masuda, Yasushi; Ishibashi, Yoshihiro; Watanabe, Takuya; Asada, Mari; Yamada, Takao; Suenaga, Masato; Kitada, Chieko; Usuki, Satoshi; Kurokawa, Tsutomu; Onda, Haruo; Nishimura, Osamu; Fujino, Masahiko
CORPORATE SOURCE: Pharmaceutical Discovery Research Division, Takeda Chemical Industries Ltd., Tsukuba, Ibaraki, 300-4293, Japan
SOURCE: Nature (London, United Kingdom) (2001), 411(6837), 613-617
CODEN: NATUAS; ISSN: 0028-0836
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Metastasis is a major cause of death in cancer patients and involves a multistep process including detachment of cancer cells from a primary cancer, invasion of surrounding tissue, spread through circulation, re-invasion and proliferation in distant organs. KiSS-1 is a human metastasis suppressor gene, that suppresses metastases of human melanomas and breast carcinomas without affecting **tumorigenicity**. However, its gene product and functional mechanisms were not elucidated. Here the authors show that KiSS-1 encodes a carboxy-terminally amidated **peptide** with 54 amino-acid residues, which the authors have isolated from human placenta as the endogenous **ligand** of an orphan G-**protein-coupled receptor** (hOT7T175) and have named 'metastin'. Metastin **inhibits** chemotaxis and invasion of hOT7T175-transfected CHO cells in vitro and attenuates pulmonary metastasis of hOT7T175-transfected B16-BL6 melanomas in vivo. The results suggest possible mechanisms of action for KiSS-1 and a potential new **therapeutic** approach.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 22 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:396891 HCAPLUS
DOCUMENT NUMBER: 135:14332
TITLE: Method of forming a peptide-receptor complex with protein zsig33 and growth hormone secretagogue

receptor (GHS-R)
INVENTOR(S): Sheppard, Paul O.; Jaspers, Stephen R.; Deisher, Theresa A.; Bishop, Paul D.
PATENT ASSIGNEE(S): Zymogenetics, Inc., USA
SOURCE: PCT Int. Appl., 111 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001038355	A2	20010531	WO 2000-US32074	20001122
WO 2001038355	A3	20011122		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-166765P P 19991122

AB The present invention relates to a method of forming a **peptide**-receptor complex with zsig33 **polypeptides** and growth hormone secretagogue receptor (GHS-R). The discovery of this novel method of forming a **peptide**-receptor complex is important for further elucidation of the how the body maintains its nutritional homeostasis and development of **therapeutics** to intervene in those processes, as well as other uses that will be apparent from the teachings herein. The present invention is based upon the identification of a previously described secreted **protein** known as zsig33 as the **peptide ligand** for an orphan receptor known as GHS-R, which belongs to G **protein-coupled receptor** family. The zsig33 **ligand** has homol. to motilin and has been found to be transcribed in the gastrointestinal system. The orphan receptor has homol. to the motilin receptor, GPR38. Anal. of the tissue distribution of the mRNA corresponding to zsig33 **protein** showed that expression was highest in stomach, followed by apparent but decreased expression levels in small intestine and pancreas. The partial sequence for the secreted zsig33 **protein** was derived from a pancreatic library, and has also been shown in lung cDNA libraries. In vitro binding studies have shown that the zsig33 **peptide** binds to kidney, duodenum, and jejunum. Thus, binding of the zsig33 **ligand** to the GHS-R is expected in tissues such as stomach, small intestine, pancreas, lung, kidney, duodenum, jejunum, and brain. Methods of **modulating** gastric contractility, nutrient uptake, growth hormones, the secretion of digestive enzymes and hormones, and/or secretion of enzymes and/or hormones in the pancreas are also included.

L20 ANSWER 23 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:319546 HCAPLUS
DOCUMENT NUMBER: 134:336698
TITLE: Protein and cDNA sequences of human **G protein-coupled receptor** PFI-013, and uses thereof in **therapy**, diagnosis, and **drug** screening

INVENTOR(S): Peter, Beate; O'Reilly, Mark Anthony
PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.
SOURCE: Eur. Pat. Appl., 66 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1096009	A1	20010502	EP 2000-309364	20001024
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
GB 2356864	A1	20010606	GB 2000-26251	20001026
JP 2001211889	A2	20010807	JP 2000-329359	20001027

PRIORITY APPLN. INFO.: GB 1999-25641 A 19991029
GB 2000-9973 A 20000420

AB This invention provides **protein** and cDNA sequences for a newly identified human **protein**, designated PFI-013, which is believed to be a **G protein-coupled receptor** . PFI-013 was identified in an expressed sequence tag (EST) database with sequences derived from a cDNA library from eosinophils **stimulated** with IL-5, but only as a partial sequence. Searching of the public genomic databases led to the identification of the full length PFI-013 sequence and the detn. of its homol. to histamine H3 receptors using, inter alia, the BLAST algorithm. Greatest level of PFI-013 mRNA expression was obsd. in peripheral blood leukocytes (PBLs) with detectable expression in spleen, testis, and colon. The likely **ligand** for PFI-013 is an amine. PFI-01 gene is mapped on human chromosome 18. The PFI-013 gene is therefore of interest because **G protein -coupled receptors** are targets of **pharmaceutical** intervention. In one embodiment, the invention relates to diagnostic assays for detecting diseases assocd. with inappropriate PFI-013 activity or levels. Also disclosed are methods for utilizing PFI-013 in **drug** screening assays and in **therapy** directed against diseases assocd. with inappropriate PFI-013 activity or levels.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 24 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:265451 HCAPLUS
DOCUMENT NUMBER: 134:290383
TITLE: Novel human **G-protein coupled receptor** for **drug** screening
INVENTOR(S): Deleersnijder, Willy; Berger, Claudia; Loeken, Christiane; Nys, Guy; Venema, Jacob
PATENT ASSIGNEE(S): Solvay Pharmaceuticals B.V., Neth.
SOURCE: PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2001025269 A2 20010412 WO 2000-EP9584 20000925
WO 2001025269 A3 20011011
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: EP 1999-203140 A 19990924
NL 1999-1013140 A 19990924
EP 2000-202683 A 20000728
US 2000-222047P P 20000731

AB The present invention relates to novel identified polynucleotides, **polypeptides** encoded by them and to the use of such polynucleotides and **polypeptides**, and to their prodn. More particularly, the polynucleotides and **polypeptides** of the present invention relate to the **G-protein coupled receptor** family, referred to as IGS4-family. The invention also relates to **inhibiting** or activating the action of such polynucleotides and **polypeptides**, to a vector contg. said polynucleotides, a host cell contg. such vector and transgenic animals where the IGS4-gene is either overexpressed, misexpressed, underexpressed or suppressed (knock-out animals). The invention further relates to a method for screening compds. capable to act as an agonist or an antagonist of said **G-protein coupled receptor** family IGS4 and the use of IGS4 **polypeptides** and polynucleotides and agonists or antagonists to the IGS4 receptor family in the treatment of PNS, psychiatric and CNS disorders, including schizophrenia, episodic paroxysmal anxiety EPA disorders such as obsessive compulsive disorder OCD, post traumatic stress disorder PTSD, phobia and panic, major depressive disorder, bipolar disorder, Parkinson's disease, general anxiety disorder, autism, delirium, multiple sclerosis, Alzheimer disease/dementia and other neurodegenerative diseases, severe mental retardation, dyskinesias, Huntington's disease, Tourett's syndrome, tics, tremor, dystonia, spasms, anorexia, bulimia, stroke, addiction/dependency/craving, sleep disorder, epilepsy, migraine; attention deficit/hyperactivity disorder (ADHD); cardiovascular diseases, including heart failure, angina pectoris, arrhythmias, myocardial infarction, cardiac hypertrophy, and hypotension. Also disclosed are hypertension - e.g., essential hypertension, renal hypertension, or pulmonary hypertension, thrombosis, arteriosclerosis, cerebral vasospasm, subarachnoid hemorrhage, cerebral ischemia, cerebral infarction, peripheral vascular disease, Raynaud's disease, kidney disease - e.g. renal failure; dyslipidemias; obesity; emesis; gastrointestinal disorders, including irritable bowel syndrome (IBS), inflammatory bowel disease (IBD), gastroesophagal reflux disease (GERD), motility disorders and conditions of delayed gastric emptying, such as post operative or diabetic gastroparesis, and diabetes, ulcers, e.g., gastric ulcer; diarrhea; other diseases including osteoporosis; inflammations; infections such as bacterial, fungal, protozoan and viral infections, particularly infections caused by HIV-1 or HIV-2; pain; cancers; **chemotherapy** induced injury; **tumor** invasion; immune disorders; urinary retention; asthma; allergies; arthritis; benign prostatic hypertrophy; endotoxin shock; sepsis; complication of diabetes mellitus; and gynaecol. disorders, among others and diagnostic assays for such conditions. Preferred uses of the invention relate to disorders of the nervous system, including the

central nervous system CNS and the peripheral nervous system PNS, disorders of the gastrointestinal system and/or of the cardiovascular system and/or of skeletal muscle and/or of the **thyroid**, and/or also to lung diseases, immunol. diseases and disorders of the genitourinary system. The invention also relates to the identification of the cognate **ligand** of the IGS4 **polypeptides** of the invention. High affinity binding to said IGS4 **polypeptides** is found for the neuropeptides known as neuromedin U.

L20 ANSWER 25 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:212153 HCAPLUS
DOCUMENT NUMBER: 135:162005
TITLE: Sphingosine 1-phosphate: An emerging **therapeutic** target
AUTHOR(S): Toman, Rachelle E.; Milstien, Sheldon; Spiegel, Sarah
CORPORATE SOURCE: Georgetown University Medical Center, Washington, DC, 20007, USA
SOURCE: Emerging Therapeutic Targets (2001), 5(1), 109-123
CODEN: ETTAF7; ISSN: 1460-0412
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review and discussion with 104 refs. Sphingosine 1-phosphate (SPP) is a polar sphingolipid metabolite that has received increasing attention as both an extracellular mediator and an intracellular second messenger. SPP is the **ligand** of a family of specific cell surface **G-protein coupled receptors** (GPCR), known as the endothelial differentiation gene-1 (EDG-1) family. These receptors, which include EDG-1, -3, -5, -6, and -8, **regulate** diverse processes including cell migration, angiogenesis, vascular maturation, heart development, neurite retraction, and soma rounding. In addn., abundant evidence indicates that SPP also acts as an intracellular lipid messenger, **regulating** calcium mobilization, cell growth, and survival. The relative intracellular level of SPP and ceramide, another sphingolipid metabolite assocd. with cell death and cell growth arrest, is an important factor in detg. cell fate. Changes in SPP and ceramide have been implicated in a no. of pathol. conditions in which apoptosis plays an important role, including cancer and neurodegenerative disorders, as well as in atherosclerosis and allergic responses. This review will examine the biosynthesis, **metab.**, and potential functions of SPP in diverse diseases in order to illuminate targets for the **pharmaceutical** and **therapeutic** manipulation of SPP levels.
REFERENCE COUNT: 104 THERE ARE 104 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 26 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:137016 HCAPLUS
DOCUMENT NUMBER: 134:173062
TITLE: Use of proteinase **inhibitor** in order to **inhibit** the cleavage of growth factor precursor
INVENTOR(S): Ullrich, Axel; Prenzel, Norbert; Daub, Henrik; Zwick-Wallasch, Esther
PATENT ASSIGNEE(S): Max-Planck-Gesellschaft zur Forderung der Wissenschaften e.V., Germany
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001012182	A1	20010222	WO 2000-EP8007	20000816

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 1999-116056 A 19990816
US 1999-461090 A 19991214

AB The invention relates to agents and methods for growth-factor receptor activation by **modulating** the **G-protein** mediated signal transduction pathway. The authors report here that activation of growth-factor receptors such as epidermal growth-factor receptor (EGFR) upon **G-protein coupled receptor** (GPCR) **stimulation** requires the receptor's extracellular domain. As key element of this mechanism the authors identify a membrane-spanning growth-factor **ligand** precursor, such as proHB-EGF, and a proteinase activity that is rapidly induced upon GPCR-**ligand** interaction. The authors show that **inhibition** of growth-factor precursor processing blocks GPCR-induced growth-factor receptor transactivation and downstream signals. As evidence for the pathophysiol. significance of this mechanism, the authors demonstrate **inhibition** of constitutive EGFR activity upon treatment of human PC-3 prostate carcinoma cells with the metalloproteinase **inhibitor** batimastat. Together, these results establish a new mechanistic concept for crosstalk among different signaling systems. Further, the results demonstrate the importance of proteinases as targets for the treatment or prevention of diseases which are assocd. with pathol. growth-factor receptor overexpression such as cancer and asthma.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 27 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:816414 HCAPLUS
DOCUMENT NUMBER: 134:110379
TITLE: Levels, **metabolism**, and **pharmacological** activity of anandamide in CB1 cannabinoid receptor knockout mice: evidence for non-CB1, non-CB2 receptor-mediated actions of anandamide in mouse brain
AUTHOR(S): Di Marzo, Vincenzo; Breivogel, Chris S.; Tao, Qing; Bridgen, David T.; Razdan, Raj K.; Zimmer, Anne M.; Zimmer, Andreas; Martin, Billy R.
CORPORATE SOURCE: Istituto per la Chimica di Molecole di Interesse Biologico, Consiglio Nazionale delle Ricerche, Arco Felice, 80072, Italy
SOURCE: Journal of Neurochemistry (2000), 75(6), 2434-2444
CODEN: JONRA9; ISSN: 0022-3042

PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Anandamide [arachidonylethanolamide (AEA)] appears to be an endogenous agonist of brain cannabinoid receptors (CB1), yet some of the neurobehavioral effects of this compd. in mice are unaffected by a selective CB1 antagonist. We studied the levels, **pharmacol.** actions, and degrdn. of AEA in transgenic mice lacking the CB1 gene. We quantified AEA and the other endocannabinoid, 2-arachidonoyl glycerol, in six brain regions and the spinal cord by isotope-diln. liq. chromatog.-mass spectrometry. The distribution of endocannabinoids and their inactivating enzyme, fatty acid amide hydrolase, were found to overlap with CB1 distribution only in part. In CB1 knockout homozygotes (CB1-/-), the hippocampus and, to a lesser extent, the striatum exhibited lower AEA levels as compared with wild-type (CB1+/+) controls. These data suggest a **ligand**/receptor relationship between AEA and CB1 in these two brain regions, where tonic activation of the receptor may tightly **regulate** the biosynthesis of its endogenous **ligand**. 2-Arachidonoyl glycerol levels and fatty acid amide hydrolase activity were unchanged in CB1-/- with respect to CB1+/+ mice in all regions, AEA and .DELTA.9-tetrahydrocannabinol (THC) were tested in CB1-/- mice for their capability of inducing analgesia and catalepsy and decreasing spontaneous activity. The effects of AEA, unlike THC, were not decreased in CB1-/- mice. AEA, but not THC, **stimulated** GTP.gamma.S binding in brain membranes from CB1-/- mice, and this **stimulation** was insensitive to CB1 and CB2 antagonists. We suggest that non-CB1, non-CB2 G **protein-coupled receptors** might mediate in mice some of the neurobehavioral actions of AEA.
REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 28 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:774242 HCAPLUS
DOCUMENT NUMBER: 134:289800
TITLE: **Pharmacology** of the eosinophil
AUTHOR(S): Giembycz, Mark A.; Lindsay, Mark A.
CORPORATE SOURCE: Thoracic Medicine, Imperial College School of Medicine at the National Heart and Lung Institute, London, SW3 6LY, UK
SOURCE: Pharmacological Reviews (1999), 51(2), 213-339
CODEN: PAREAQ; ISSN: 0031-6997
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 1930 refs. Topics discussed include an historical perspective; life cycle, maturation, and tissue distribution; transcription factors and eosinophils; G **protein-coupled receptors** and their **ligands**; interleukin-3, interleukin-5, and granulocyte/macrophage colony-**stimulating** factor; the interferon receptor superfamily; the **tumor** necrosis factor superfamily; adhesion mols.; Igs; the functional consequences of eosinophil activation; eosinophil heterogeneity; and **pharmacol. modulation** of eosinophil function.
REFERENCE COUNT: 1774 THERE ARE 1774 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 29 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:445772 HCAPLUS
DOCUMENT NUMBER: 133:171945
TITLE: Identification and characterization of potent, selective, and orally active antagonist of the CC chemokine receptor-1
AUTHOR(S): Liang, Meina; Mallari, Cornell; Rosser, Mary; Ng, Howard P.; May, Karen; Monahan, Sean; Bauman, John G.; Islam, Imadul; Ghannam, Ameen; Buckman, Brad; Shaw, Ken; Wei, Guo-Ping; Xu, Wei; Zhao, Zuchun; Ho, Elena; Shen, Jun; Oanh, Huynh; Subramanyam, Babu; Vergona, Ron; Taub, Dennis; Dunning, Laura; Harvey, Susan; Snider, R. Michael; Hesselgesser, Joseph; Morrissey, Michael M.; Perez, H. Daniel; Horuk, Richard
CORPORATE SOURCE: Department of Discovery Research, Berlex Biosciences, Richmond, CA, 94804, USA
SOURCE: Journal of Biological Chemistry (2000), 275(25), 19000-19008
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The CC chemokine receptor-1 (CCR1) is a prime **therapeutic** target for treating **autoimmune** diseases. Through high capacity screening followed by chem. optimization, we identified a novel non-**peptide** CCR1 antagonist, R-N-[5-chloro-2-[2-[4-[(4-fluorophenyl)methyl]-2-methyl-1-pipera zinyl]-2-oxoethoxy]phenyl]urea hydrochloric acid salt (BX 471). Competition binding studies revealed that BX 471 was able to displace the CCR1 **ligand** macrophage inflammatory **protein**-1.alpha. (MIP-1.alpha.), RANTES, and monocyte chemotactic **protein**-3 (MCP-3) with high affinity (Ki ranged from 1 nM to 5.5 nM). BX 471 was a potent functional antagonist based on its ability to **inhibit** a no. of CCR1-mediated effects including Ca2+ mobilization, increase in extracellular acidification rate, CD11b expression, and leukocyte migration. BX 471 demonstrated a greater than 10,000-fold selectivity for CCR1 compared with 28 **G-protein-coupled receptors**.
Pharmacokinetic studies demonstrated that BX 471 was orally active with a bioavailability of 60% in dogs. Furthermore, BX 471 effectively reduces disease in a rat exptl. allergic encephalomyelitis model of multiple sclerosis. This study is the first to demonstrate that a non-**peptide** chemokine receptor antagonist is efficacious in an animal model of an **autoimmune** disease. In summary, we have identified a potent, selective, and orally available CCR1 antagonist that may be useful in the treatment of chronic inflammatory diseases.
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 30 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:384230 HCAPLUS
DOCUMENT NUMBER: 133:38254
TITLE: Novel physiologically active substance, process for producing the same and utilization thereof
INVENTOR(S): Mori, Masaaki; Abe, Michiko; Shimomura, Yukio; Sugo, Tsukasa; Kitada, Chieko
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 147 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000032627	A1	20000608	WO 1999-JP6649	19991129
W: AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CR, CU, CZ, DM, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MA, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
JP 2001128688	A2	20010515	JP 1999-338410	19991129
EP 1136503	A1	20010926	EP 1999-973037	19991129
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.:
JP 1998-338984 A 19981130
JP 1999-26848 A 19990204
JP 1999-239367 A 19990826
WO 1999-JP6649 W 19991129

AB A novel peptide recognized as a ligand by a G protein-coupled receptor protein. The above peptide is usable in: (1) developing a receptor-bonded assay system and screening a candidate compd. for a drug with the use of a recombinant receptor protein expression system; and (2) developing drugs such as a central function controlling agent, a circulatory function controlling agent, a heart function controlling agent, an immunol. function controlling agent, a digestive function controlling agent, a metabolic function controlling agent or a genital function controlling agent.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 31 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:227678 HCAPLUS
DOCUMENT NUMBER: 132:279545
TITLE: Preparation of peptide derivatives with binding activity for APJ receptor
INVENTOR(S): Kitada, Chieko; Hinuma, Shuji
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 116 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000018793	A1	20000406	WO 1999-JP5216	19990924
W: AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CR, CU, CZ, DM, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ,				

MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9957593	A1	20000417	AU 1999-57593	19990922
JP 2000159795	A2	20000613	JP 1999-270419	19990924
EP 1116727	A1	20010718	EP 1999-944809	19990924

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.: JP 1998-271626 A 19980925
WO 1999-JP5216 W 19990924

OTHER SOURCE(S): MARPAT 132:279545

AB Prepd. are novel **peptides** represented by formula X1-Arg-Pro-Arg-X2-Ser-His-X3-Gly-Pro-X4-X5 [X1 = H, amino acid or **peptide** consisting of 1-25 amino acids optionally substituted in side chains; X2 = neutral amino acid residue optionally substituted in side chains; X3 = neutral, arom., or basic amino acid residue optionally substituted in side chains; X4 = bond, neutral or arom. amino acid residue optionally substituted in side chains; X5 = (1) amino acid residue optionally substituted in side chains or its deriv. formed by reducing the C-terminus CO2H to CH2OH or CHO, (2) HO, or (3) amino acid or dipeptide residue optionally substituted in side chains or its deriv. formed by reducing the C-terminus CO2H to CH2OH or CHO; wherein Arg-Pro-Arg, Ser-His, or Gly-Pro is optionally substituted in side chains; excluding the **peptide** where X2 = Leu, X3 = Lys, X4 = Met, and X5 = Pro or Pro-Phe and Arg-Pro-Arg, Ser-His, and Gly-Pro are not substituted] which is recognized as a **ligand** by a **G protein-coupled receptor protein**. These **peptides** are usable in: (1) developing a receptor-binding assay system with the use of an expression system of a recombinant receptor **protein** and screening candidates for **drugs**; and (2) developing **drugs** such as central function controlling agents, circulatory function controlling agents, heart function controlling agents, immune function controlling agents, digestive function controlling agents, metabolic function controlling agents or reproductive function controlling agents. Thus, Arg-Pro-Arg-Leu-Ser-His-Lys-Gly-Pro-Met-Phe(Cl)-OH, which was prepd. by the solid phase synthesis, showed ED50 of 0.10 nM for **inhibiting** the phosphocholine-**stimulated** cAMP prodn. in CHO-A10 clone 6 cells.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 32 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:207381 HCAPLUS
DOCUMENT NUMBER: 133:12934
TITLE: Molecular **pharmacology** of human vasopressin receptors
AUTHOR(S): Thibonnier, Marc; Conarty, Doreen M.; Preston, Judith A.; Wilkins, Pamela L.; Berti-Mattera, Liliana N.; Mattera, Rafael
CORPORATE SOURCE: Division of Clinical and Molecular Endocrinology, Department of Medicine, Case Western Reserve University School of Medicine, Cleveland, OH, 44106-4951, USA
SOURCE: Advances in Experimental Medicine and Biology (1998), 449(Vasopressin and Oxytocin), 251-276
CODEN: AEMBAP; ISSN: 0065-2598
PUBLISHER: Plenum Press
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Vasopressin (AVP) and oxytocin (OT) are cyclic nonapeptides whose actions are mediated by activation of specific **G protein-coupled receptors** (GPCRs) currently classified into V1-vascular (V1R), V2-renal (V2R) and V3-pituitary (V3R) AVP receptors and OT receptors (OTR). The cloning of the different members of the AVP/OT family of receptors now allows the extensive mol. **pharmacol.** characterization of a single AVP/OT receptor subtype in stably transfected mammalian cell lines. The human V1-vascular (CHO-V1), V2-renal (CHO-V2), V3-pituitary (CHO-V3) and oxytocin (CHO-OT) receptors stably expressed in CHO cells display distinct binding profiles for 18 **peptide** and 5 nonpeptide AVP/OT analogs. Several **peptide** and nonpeptide compds. have a greater affinity for the V1R than AVP itself. V2R **peptide** agonists and antagonists tend to be non-selective **ligands**, whereas nonpeptide V2R antagonists are potent and subtype-selective. None of the 22 AVP/OT analogs tested has a better affinity for the human V3R than AVP itself. Several **peptide** antagonists do not select well between V1R and OTR. These results underscore the need for developing specific and potent analogs interacting specifically with a given human AVP/OT receptor subtype. The authors measured thymidine uptake as an index of mitogenic activity elicited by activation of a given AVP/OT receptor subtype. **Stimulation** of V1Rs, V3Rs by AVP as well as OTRs by OT produces a dose-dependent mitogenic response, whereas AVP occupancy of V2Rs leads to an anti-mitogenic response. For similar levels of expression of receptors, the mitogenic efficacy is ranked as follows: V1Rs > V3Rs > OTRs. Deletion of the C-terminus of the human V1R which contains four PKC phosphorylation sites abolishes the mitogenic effect of AVP. The authors directly measured AVP- or OT-**stimulated** formation of cAMP in CHO-V1, CHO-V2, CHO-V3, and CHO-OT cells and the results suggest that only the AVP/OT receptor subtypes which do not **stimulate** cAMP prodn. (V1R, V3Rs, and OTRs) increase thymidine uptake. The mitogen-activated **protein** kinases (MAPKs) are a point of convergence for mitogenic signals triggered by several classes of cell surface receptors including the GPCRs. AVP-dependent activation of MAPKs was examd. in CHO cells transfected with the various AVP receptor subtypes. Activation of all AVP receptor subtypes produces a dose-dependent phosphorylation of p42 and p44 MAPKs which peaked at 10 min, started to decay slowly afterwards in all cell types, but lasted for at least 2 h. Since the various AVP receptor subtypes show a differential **G protein** coupling profile, **stimulation** of MAP kinase phosphorylation by the various types of AVP receptors suggests that different pathways are involved in the process. In CHO-V3 cells stably expressing low, medium or high levels of human V3Rs (Bmax: <10 pmol/mg, 10 to 25 pmol/mg, and 25 to 100 pmol/mg, resp.), AVP **stimulation** of phospholipase C, phospholipase A2, [3H]thymidine uptake, cAMP prodn., MAP kinases phosphorylation was a function of the receptor d. The V3R activates several signaling pathways via different **G proteins**, depending on the level of receptor expression. The increased synthesis of DNA and cAMP levels obsd. in cells expressing medium and high levels of V3Rs, resp., may represent important events in the **tumorigenesis** of corticotroph cells.

REFERENCE COUNT: 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 33 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:768892 HCAPLUS
DOCUMENT NUMBER: 132:73739
TITLE: Receptors for PTH and PTHrP: their biological

importance and functional properties
AUTHOR(S): Mannstadt, Michael; Juppner, Harald; Gardella, Thomas J.
CORPORATE SOURCE: Endocrine Unit, Department of Medicine, Massachusetts General Hospital and Harvard Medical School, Boston, MA, 02114, USA
SOURCE: Am. J. Physiol. (1999), 277(5, Pt. 2), F665-F675
CODEN: AJPHAP; ISSN: 0002-9513
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 123 refs. The type 1 receptor (PTH1R) for **parathyroid** hormone (PTH) and **parathyroid** hormone-related **peptide** (PTHrP) is a **G protein -coupled receptor** that is highly expressed in bone and kidney and mediates in these tissues the PTH-dependent **regulation** of mineral ion homeostasis. The PTH1R also mediates the paracrine actions of PTHrP, which play a particularly vital role in the process of endochondral bone formation. These important functions, the likely involvement of the PTH1R in certain genetic diseases affecting skeletal development and calcium homeostasis, and the potential utility of PTH in treating osteoporosis have been the driving force behind intense investigations of both the receptor and its **peptide ligands**. Recent lines of work have led to the identification of constitutively active PTH1Rs in patients with Jansen's metaphyseal chondrodysplasia, the demonstration of inverse agonism by certain **ligand** analogs, and the discovery of the PTH-2 receptor subtype that responds to PTH but not PTHrP. As reviewed herein, a detailed exploration of the receptor-**ligand** interaction process is currently being pursued through the use of site-directed mutagenesis and photoaffinity crosslinking methods; ultimately, such work could enable the development of novel PTH receptor **ligands** that have **therapeutic** value in treating diseases such as osteoporosis and certain forms of hypercalcemia.
REFERENCE COUNT: 125 THERE ARE 125 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 34 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:610347 HCAPLUS
DOCUMENT NUMBER: 132:121434
TITLE: Purinergic receptor **modulation** of LPS-**stimulated** signaling events and nitric oxide release in RAW 264.7 macrophages
AUTHOR(S): Sommer, J. A.; Fisette, P. L.; Hu, Y.; Denlinger, L. C.; Guerra, A. N.; Bertics, P. J.; Proctor, R. A.
CORPORATE SOURCE: Department of Biomolecular Chemistry, University of Wisconsin Medical School, Madison, WI, 53706, USA
SOURCE: J. Endotoxin Res. (1999), 5(1/2), 70-74
CODEN: JENREB; ISSN: 0968-0519
PUBLISHER: Maney Publishing
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Purinergic receptors of the P2 class are cell surface receptors which are sensitive to extracellular adenine nucleotides, such as ATP and ADP. This class of receptors is divided into the P2Y family of **G protein-coupled receptors** and the P2X family of **ligand**-gated ion channels. The P2X receptors, seven of which have been cloned, are thought to possess two transmembrane domains and

function as multimeric complexes. Numerous studies have suggested a role for P2 receptors in activation of macrophages by Gram-neg. bacterial endotoxin (lipopolysaccharide; LPS). LPS is thought to exert its toxic effects, in large part, by inducing macrophages to release inflammatory mediators such as **tumor** necrosis factor .alpha. (TNF.alpha.), interleukin-1 (IL-1) and nitric oxide (NO). Although multiple signal transduction pathways are activated by LPS in macrophages, the proximal mechanisms by which LPS exerts these effects remain unclear. The current study examines the role of the P2X7/P2Z purinergic receptor in LPS signaling events and in nitric oxide (NO) prodn. The results indicate that the P2X7 receptor is reguired for maximal LPS activation of the mitogen-activated **protein** (MAP) kinases extracellular signal-**regulated** kinase (ERK)1 and ERK2, for activation of nuclear factor (NF)-.kappa.B, as well as for upregulation of the inducible form of nitric oxide synthase (iNOS). These results are fortified by our recent observation that the C-terminus of the P2X7 receptor is homologous to conserved LPS binding domains of **proteins** crit. to host responses to Gram-neg. bacterial infection, such as LPS-binding **protein** (LBP) and bactericidal permeability-increasing **protein** (BPI). Taken together, these observations suggest that the P2X7 receptor plays a fundamental role in LPS signal transduction and activation of macrophages, and thus may represent a **therapeutic** target for Gram-neg. bacterial septicemia.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 35 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:464081 HCAPLUS
DOCUMENT NUMBER: 131:99051
TITLE: Mammalian apelin **ligands** for the orphan **G protein-coupled** **receptor** APJ and their cDNA sequences
INVENTOR(S): Hinuma, Shuji; Tatemoto, Kazuhiko; Hosoya, Masaki; Habata, Yugo; Fujii, Ryo; Kitada, Chieko
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 169 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9933976	A1	19990708	WO 1998-JP5805	19981222
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9916854	A1	19990719	AU 1999-16854	19981222
JP 2000159798	A2	20000613	JP 1998-364656	19981222
EP 1040189	A1	20001004	EP 1998-961474	19981222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: JP 1997-353955 A 19971224
JP 1998-32577 A 19980216

JP 1998-220853 A 19980804
JP 1998-271645 A 19980925
WO 1998-JP5805 W 19981222

AB A peptide ligand, designated apelin, for the orphan G protein-coupled receptor APJ is provided. The cDNAs encoding the 77-residue preproapelin are provided from human, mouse, rat, and bovine sources. Synthetic peptides derived from the C-terminal amino acid sequence of preproapelin are capable of specifically promoting the acidification rate in cells expressing the APJ receptor in a range from 10-7 to 10-10M, indicating that apelin in an endogenous ligand for the APJ receptor. This invention relates to a polypeptide involving the modulation of central nervous system function, circulatory function, immune function, gastrointestinal function, metabolic function, reproductive function, etc., it can be used as a drug for treating or preventing a variety of diseases, e.g. HIV infection or AIDS (acquired immune deficiency syndrome) or the like.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 36 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:316394 HCAPLUS
DOCUMENT NUMBER: 131:125517
TITLE: Molecular physiology of the gonadotropin-releasing hormone (GnRH) receptor
AUTHOR(S): Kakar, Sham S.; Williams, Iantha; Jennes, Lothar
CORPORATE SOURCE: Department of Physiology and Biophysics, University of Alabama at Birmingham, Birmingham, AL, 35294-0005, USA
SOURCE: Adv. Reprod. (1999), 3(3,4), 267-278
CODEN: AREPFL
PUBLISHER: Reproductive Health Center
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review, with 45 refs. Gonadotropin releasing hormone (GnRH), through its G-protein-coupled, high-affinity receptors located on gonadotropes of the anterior pituitary, stimulates the secretion of gonadotropins (LH and FSH). It is now known that GnRH receptors (GnRHR) are also present in extra-pituitary tissues, hormone-responsive tumors and tumor-derived cell lines, suggesting that GnRH may serve addnl. functions. GnRHR expression is highly regulated in exhibiting both up and down regulation by its cognate ligand, by gonadal steroids and peptides. However, the mechanisms involved in altering the rate of expression of the GnRHR at mol. level are unknown. In order to understand the regulation of GnRHR gene expression in the pituitary, extra-pituitary tissues and hormone responsive tumors , we cloned and sequenced the high affinity GnRH receptor from human pituitary gland, a breast tumor cell line (MCF-7), and from an ovarian tumor and defined its primary structure. GnRH receptor from the human pituitary, which binds GnRH with high affinity, is a 328 amino acids protein and belongs to the family of 7-transmembrane G-protein-coupled receptors. It utilizes Ca2+ as a second messenger. Nucleotide sequencing of the GnRH receptors isolated from MCF-7 and from an ovarian tumor showed complete identity with that of human pituitary GnRH receptor. We also demonstrated for the first time that GnRH receptor mRNA is expressed in various normal human tissues in addn. to the pituitary and hormone-dependent tumors incIuding breast, prostate, and ovarian tumors and tumor-derived cell lines, suggesting an

important role of GnRH/GnRH in **regulation** of **tumor** cell growth and proliferation. Further studies will facilitate the development of new **therapeutic** approach for cancer **therapy** and understanding the complex mechanism of LH secretion from the gonadotropes.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 37 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:237833 HCAPLUS
DOCUMENT NUMBER: 131:39047
TITLE: **Therapeutic** applications of ATP-(P2)-receptors agonists and antagonists
AUTHOR(S): Fischer, Bilha
CORPORATE SOURCE: Gonda-Goldschmied Medical Research Center, Department of Chemistry, Bar-Ilan University, Ramat-Gan, 52900, Israel
SOURCE: Expert Opin. Ther. Pat. (1999), 9(4), 385-399
CODEN: EOTPEG; ISSN: 1354-3776
PUBLISHER: Ashley Publications
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 87 refs. P2-receptors (P2-R), which recognize extracellular ATP, represent significant targets for novel **drug** development regarding different pathophysiol. conditions. In recent years, approx. fifteen ATP receptor subtypes have been cloned; seven of which belong to the P2X-R family (**ligand**-gated-ion-channel receptors). The remaining subtypes belong to the P2Y-R family (**G-protein coupled receptors**). These receptors have been classified based on their putative mol. structure, function, and the action of a subtype selective **drug** on the cloned receptor. A limited no. of reports describe the identification of potent and selective P2X/P2Y agonists, thus extending the restricted arsenal of P2-R agonists consisting primarily of com. compds. Several new and subtype selective antagonists have been recently identified which open a new avenue of P2X or P2Y subtype selective antagonists for receptor studies. Current applications of P2-R agonists and antagonists include their use as insulin secretagogues, **inhibitors** of ADP-induced platelet aggregation, agents for hydration of lung mucous in cystic fibrosis (CF) patients, **modulators** of cardiac muscle contractility, and antineoplastic agents. This paper reviews selected P2-R related publications and patents issued between 1995 and 1998 for newly cloned P2-R, **drug** candidates, and the potential **therapeutic** applications of the **drugs**.

REFERENCE COUNT: 87 THERE ARE 87 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 38 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:763141 HCAPLUS
DOCUMENT NUMBER: 130:90728
TITLE: The mouse Galr2 galanin receptor: genomic organization, cDNA cloning, and functional characterization
AUTHOR(S): Pang, Ling; Hashemi, Tanaz; Lee, Hu-Jung J.; Maguire, Maureen; Graziano, Michael P.; Bayne, Marvin; Hawes, Brian; Wong, Gwendolyn; Wang, Suke
CORPORATE SOURCE: Department of CNS/CV Biological Research, Schering-Plough Research Institute, Kenilworth, NJ, 07033, USA

SOURCE: J. Neurochem. (1998), 71(6), 2252-2259
CODEN: JONRA9; ISSN: 0022-3042
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The diverse physiol. actions of galanin are thought to be mediated through activation of galanin receptors (GalRs). The authors report the genomic and cDNA cloning of a mouse Gal1R that possesses a genomic structure distinct from that of Gal1R1 and encodes a functional galanin receptor. The mouse Gal1R gene consists of two exons sepd. by a single intron within the **protein-coding** region. The splicing site for the intron is located at the junction between the third transmembrane domain and the second intracellular loop. The cDNA encodes a 370-amino acid putative **G protein-coupled receptor** that is markedly different from human Gal1R1 and rat Gal1R3 (38 and 57%) but shares high homol. with rat Gal1R2 (94%). In binding studies utilizing membranes from COS-7 cells transfected with mouse Gal1R2 cDNA, the receptor displayed high affinity (KD = 0.47 nM) and saturable binding with 125I-galanin (Bmax = 670 fmol/mg). The radioligand binding can be displaced by galanin and its analogs in a rank order: galanin .simeg. M40 .simeg. M15 .simeq. M35 .simeq. C7 .simeq. galanin(2-29) .mchgt. galanin (1-16) .mchgt. galanin(10-29) .simeq. galanin(3-29), which resembles the **pharmacol**. profile of the rat Gal1R2. Receptor activation by galanin in COS-7 cells **stimulated** phosphoinositide **metab**., which was not reversed by pertussis toxin. Thus, the galanin receptor encoded in the cloned mouse Gal1R gene is the type 2 galanin receptor and is active in both **ligand** binding and signaling assays.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 39 OF 48 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:503328 HCAPLUS
DOCUMENT NUMBER: 129:199552

TITLE: Small molecular probes for G-protein-coupled C5a receptors. Conformationally constrained antagonists derived from the C terminus of the human plasma protein C5a

AUTHOR(S): Wong, Allan K.; Finch, Angela M.; Pierens, Gregory K.; Craik, David J.; Taylor, Stephen M.; Fairlie, David P.
CORPORATE SOURCE: Centre for Drug Design and Development, University of Queensland, Brisbane, 4072, Australia

SOURCE: J. Med. Chem. (1998), 41(18), 3417-3425
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Activation of the human complement system of blood plasma **proteins** in response to infection or injury produces a 4-helix bundle glycoprotein (74 amino acids) known as C5a. C5a binds to **G-protein -coupled receptors** on cell surfaces triggering receptor-**ligand** internalization, signal transduction, and powerful inflammatory responses. Since excessive levels of C5a are assocd. with **autoimmune** and chronic inflammatory disorders, **inhibitors** of receptor activation may have **therapeutic** potential. The authors report soln. structures and receptor-binding and antagonist activities for some of the 1st small mol. antagonists of C5a derived from its hexapeptide C terminus. The antagonist NMe-Phe-Lys-Pro-D-Cha-Trp-D-Arg-CO2H (I) surprisingly shows an unusually well-defined soln. structure as detd. by 1H NMR spectroscopy. This is one

of the smallest acyclic **peptides** found to possess a defined soln. conformation, which can be explained by the constraining role of intramol. H bonding. NOE and coupling const. data, slow D2 exchange, and a low dependence on temp. for the chem. shift of the D-Cha-NH strongly indicate an inverse .gamma. turn stabilized by a D-Cha-NH.cntdot..cntdot..cntdot.OC-Lys H bond. Smaller conformational populations are assocd. with a H bond between Trp-NH.cntdot..cntdot..cntdot.OC-Lys, defining a type II .beta. turn distorted by the inverse .gamma. turn incorporated within it. An excellent correlation between receptor-affinity and antagonist activity is indicated for a limited set of synthetic **peptides**. Conversion of the C-terminal carboxylate of I to an amide decreases antagonist potency 5-fold, but potency is increased .ltoreq.10-fold over I if the amide bond is made between the C-terminal carboxylate and a Lys/Orn side chain to form a cyclic analog. The soln. structure of cycle 6 also shows .gamma. and .beta. turns; however, the latter occurs in a different position, and there are clear conformational changes in 6 vs I that result in enhanced activity. These results indicate that potent C5a antagonists can be developed by targeting site 2 alone of the C5a receptor and define a novel **pharmacophore** for developing powerful receptor probes or **drug** candidates.

L20 ANSWER 40 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:463702 HCAPLUS
DOCUMENT NUMBER: 129:187130
TITLE: Structural and functional aspects of **G protein-coupled receptor** oligomerization
AUTHOR(S): Hebert, Terence E.; Bouvier, Michel
CORPORATE SOURCE: Centre de Recherche, Institut de Cardiologie de Montreal et Departement d'anesthesie-reanimation, Universite de Montreal, Montreal, QC H1T 1C8, Can.
SOURCE: Biochem. Cell Biol. (1998), 76(1), 1-11
CODEN: BCBIEQ; ISSN: 0829-8211
PUBLISHER: National Research Council of Canada
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 82 refs. **G protein-coupled receptors** (GPCRs) represent the single largest family of cell surface receptors involved in signal transduction. It is estd. that several hundred distinct members of this receptor family in humans direct responses to a wide variety of chem. transmitters, including biogenic amines, amino acids, **peptides**, lipids, nucleosides, and large **polypeptides**. These transmembrane receptors are key controllers of such diverse physiol. processes as neurotransmission, cellular **metab.**, secretion, cellular differentiation, and growth as well as inflammatory and immune responses. GPCRs therefore represent major targets for the development of new **drug** candidates with potential application in all clin. fields. Many currently used **therapeutics** act by either activating (agonists) or blocking (antagonists) GPCRs. Studies over the past two decades have provided a wealth of information on the biochem. events underlying cellular signalling by GPCRs. However, our understanding of the mol. interactions between **ligands** and the receptor **protein** and, particularly, of the structural correlates of receptor activation or **inhibition** by agonists and inverse agonists, resp., is still rudimentary. Most of the work in this area has focused on mapping regions of the receptor responsible for **drug** binding affinity. Although binding of **ligand** mols. to specific receptors represents the

first event in the action of **drugs**, the efficacy with which this binding is translated into a physiol. response remains the only determinant of **therapeutic** utility. In the last few years, increasing evidence suggested that receptor oligomerization and in particular dimerization may play an important role in the mol. events leading to GPCR activation. In this paper, we review the biochem. and functional evidence supporting this notion.

L20 ANSWER 41 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:184011 HCAPLUS
DOCUMENT NUMBER: 128:242903
TITLE: Human CXC chemokine receptor 3, its cDNA sequence, and its diagnostic and **therapeutic** uses
INVENTOR(S): Loetscher, Marcel; Moser, Bernhard; Qin, Shixin; Mackay, Charles R.
PATENT ASSIGNEE(S): Theodor-Kocher Institute, Switz.; Leukosite, Inc.
SOURCE: PCT Int. Appl., 137 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9811218	A1	19980319	WO 1997-US15915	19970910
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6140064	A	20001031	US 1996-709838	19960910
US 6184358	B1	20010206	US 1997-829839	19970331
AU 9742608	A1	19980402	AU 1997-42608	19970910
AU 734090	B2	20010607		
EP 925358	A1	19990630	EP 1997-940941	19970910
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.:
US 1996-709838 A 19960910
US 1997-829839 A 19970331
WO 1997-US15915 W 19970910

AB The present invention relates to recombinant chemokine designated CXC Chemokine Receptor 3 (CXCR3) that is selective for the CXC chemokines IP-10 (interferon .gamma.-inducible 10-kDa **protein**) and Mig (monokine induced by .gamma.-interferon), and/or the ability to induce a cellular response (e.g., chemotaxis, exocytosis). The cDNA clone which was isolated from a human CD4+ T cell library, was not detected in monocyte- or granulocyte-derived cDNA libraries. Sequence anal. of the clone revealed an open reading frame of 1104 bp, encoding a predicted **protein** of 368 amino acids with a predicted mol. mass of 40,659 Da. The amino acid sequence includes 7 putative transmembrane segments which are characteristic of **G-protein coupled receptors** and are found in other chemoattractant receptors. Consistent with this observation, the receptor mediates Ca2+ mobilization and chemotaxis in response to IP-10 and Mig. Lymphocytes, particularly T lymphocytes, bearing a CXCR3 receptor as a result of activation can be

recruited into inflammatory lesions, sites of infection, or **tumors** by IP-10 and/or Mig, which can be induced locally by interferon-.gamma.. Thus, CXCR3 plays a role in the selective recruitment of lymphocytes, particularly effector cells such as activated or **stimulated** T lymphocytes. Another aspect of the invention relates to antisense nucleic acid, recombinant nucleic acid constructs, such as plasmids or retroviral vectors, methods of identifying **ligands**, and **inhibitors** (e.g., antagonists) or promoters (e.g., agonists) of receptor function.

L20 ANSWER 42 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:97341 HCAPLUS
DOCUMENT NUMBER: 128:188656
TITLE: Growth hormone-releasing peptides and their analogs
AUTHOR(S): Camanni, Franco; Ghigo, Ezio; Arvat, Emanuela
CORPORATE SOURCE: Department of Internal Medicine, Division of Endocrinology, University of Turin, 10126, Italy
SOURCE: Front. Neuroendocrinol. (1998), 19(1), 47-72
CODEN: FNEDA7; ISSN: 0091-3022
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review, with 172 refs. Growth hormone-releasing **peptides** (GHRPs) are a series of hepta (GHRP-1)- and hexapeptides (GHRP-2, GHRP-6, Hexarelin) that have been shown to be effective releasers of GH in animals and humans. More recently, a series of nonpeptidyl GH secretagogues (L-692,429, L-692,585, MK-0677) were discovered using GHRP-6 as a template. Some cyclic **peptides** as well as penta-, tetra-, and pseudotripeptides have also been described. This review summarizes recent developments in our understanding of the GHRPs, as well as the current nonpeptide **pharmacol**. analogs. GHRPs and their analogs have no structural homol. with GHRH and act via specific receptors present at either the pituitary or the hypothalamic level. The GHRP receptor has recently been cloned and it does not show sequence homol. with other G-**protein-coupled receptors** known so far. This evidence strongly suggests the existence of a natural GHRP-like **ligand** which, however, has not yet been found. Although the exact mechanism of action of GHRPs has not been fully established, there is probably a dual site of action on both the pituitary and the hypothalamus, possibly involving **regulatory** factors in addn. to GHRH and somatostatin. Moreover, the possibility that GHRPs act via an unknown hypothalamic factor (U factor) is still open. The marked GH-releasing activity of GHRPs is reproducible and dose-related after i.v., s.c., intranasal, and even oral administration. The GH-releasing effect of GHRPs is the same in both sexes, but undergoes age-related variations. It increases from birth to puberty and decreases in aging. The GH-releasing activity of GHRPs is synergistic with that of GHRH and not affected by opioid receptor antagonists, while it is only blunted by **inhibitory** influences that are known to nearly abolish the effect of GHRH, such as neurotransmitters, glucose, free fatty acids, glucocorticoids, rhGH, and even exogenous somatostatin. GHRPs maintain their GH-releasing effect in somatotrope hypersecretory states, such as **acromegaly**, anorexia nervosa, and **hyperthyroidism**. On the other hand, GHRPs and their analogs have been reported to be effective in idiopathic short stature, in some situations of GH deficiency, in obesity, and in **hypothyroidism**, while in patients with pituitary stalk disconnection and in Cushing's syndrome the somatotrope responsiveness to GHRPs is almost absent. A potential role in the treatment of short stature, aging, catabolic states, and dilated cardiomyopathy has been envisaged.

L20 ANSWER 43 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:15848 HCAPLUS
DOCUMENT NUMBER: 128:84749
TITLE: A type II gonadotropin-releasing hormone receptor from human and the gene encoding it and the development of effectors of the receptor
INVENTOR(S): Millar, Robert; Conklin, Darrell C.; Hapgood, Janet; Rumbak, Elaine; Troskie, Brigitte; Illing, Nicola
PATENT ASSIGNEE(S): Zymogenetics, Inc., USA; University of Cape Town
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9747743	A1	19971218	WO 1997-US10144	19970611
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9733885	A1	19980107	AU 1997-33885	19970611
ZA 9705195	A	19971215	ZA 1997-5195	19970612

PRIORITY APPLN. INFO.: US 1996-19733P P 19960613
WO 1997-US10144 W 19970611

AB A human gonadotropin-releasing hormone receptor, is identified and characterized and the gene encoding it is cloned. The **polypeptide** has **G protein-coupled receptor** characteristics and, based on homol. to other mammalian gonadotropin-releasing hormone receptors, appears to be the receptor for the conserved GnRH II **ligand**. The **polypeptide** may be used to detect the natural human **ligand** and **ligand** analogs. The receptor can also be used in methods to influence sexual behavior and reduce proliferation of **tumor** cells. The gene was cloned using primers derived from an expressed sequence tag that had sequence features indicating that it encoded a gonadotropin receptor to generate a probe that was then used to screen a human P1 library.

L20 ANSWER 44 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:696874 HCAPLUS
DOCUMENT NUMBER: 127:355666
TITLE: Manufacture of soluble anterior pituitary hormone receptors as cleavable fusion products with a membrane anchor peptide
INVENTOR(S): Hsueh, Aaron J. W.; Kobilka, Brian K.; Kudo, Masataka
PATENT ASSIGNEE(S): Leland Stanford Junior University, USA
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9739131	A1	19971023	WO 1997-US6117	19970414
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2250975	AA	19971023	CA 1997-2250975	19970414
AU 9727282	A1	19971107	AU 1997-27282	19970414
EP 910648	A1	19990428	EP 1997-921166	19970414
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 5925549	A	19990720	US 1997-837151	19970414
JP 2001519650	T2	20011023	JP 1997-537262	19970414

PRIORITY APPLN. INFO.: US 1996-15450P P 19960415
WO 1997-US6117 W 19970414

AB A method of manufg. the extracellular domain of 7-transmembrane domain **G-protein coupled receptor**, specifically a glycoprotein hormone receptor, in a form that can be easily solubilized is described. The solubilized **ligand** binding domains have a no. of **therapeutic** uses. The domain is manufd. as a fusion **protein** with a membrane anchor domain appropriate for the expression host with a cleavable **peptide** linker. The domain can then be released by treatment with a cleavage reagent, specifically a proteinase. Manuf. of LH, FSH, and TSH as fusion products with CD8 antigen using 293 cells as expression hosts for pCDNA-derived expression constructs is described. The FSH receptor fusion **protein** retained a high affinity for FSH and the sol. extracellular domain **inhibited** FSH action in vitro. The **protein** was also able to induce apoptosis in rat testis cells upon injection.

L20 ANSWER 45 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:505465 HCAPLUS
DOCUMENT NUMBER: 117:105465
TITLE: Molecular cloning of a human cannabinoid receptor which is also expressed in testis
AUTHOR(S): Gerard, Catherine M.; Mollereau, Catherine; Vassart, Gilbert; Parmentier, Marc
CORPORATE SOURCE: Fac. Med., Univ. Libre Bruxelles, Brussels, 1070, Belg.
SOURCE: Biochem. J. (1991), 279(1), 129-34
CODEN: BIJOAK; ISSN: 0306-3275
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A cDNA clone encoding a receptor **protein** which presents all the characteristics of a guanine-nucleotide-binding **protein** (**G-protein)-coupled receptor** was isolated from a human brain stem cDNA library. The probe used (HGMP08) was a 600 bp DNA fragment amplified by a low-stringency polymerase chain reaction (PCR), using human genomic DNA as template and degenerate oligonucleotide primers corresponding to conserved sequences amongst the known **G-protein-coupled receptors**. The deduced amino acid sequence encodes a **protein** of 472 residues which shares 97.3% identity with the rat cannabinoid receptor cloned recently [Matsuda, L. A., et al., (1990)]. Abundant transcripts were detected in the brain, as expected, but lower amts. were also found in the testis. The same probe was used to screen a human testis cDNA library. The cDNA clones obtained were partially sequenced, demonstrating the identity of the cannabinoid receptors expressed in both tissues.

Specific binding of the synthetic cannabinoid **ligand** [3H]CP55940 was obsd. on membranes from Cos-7 cells transfected with the recombinant receptor clone. In stably transfected CHO-K1 cell lines, cannabinoid agonists mediated a dose-dependent and stereoselective **inhibition** of forskolin-induced cAMP accumulation. The ability to express the human cannabinoid receptor in mammalian cells should help in developing more selective **drugs**, and should facilitate the search for the endogenous cannabinoid **ligand**(s).

L20 ANSWER 46 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:229469 HCAPLUS
DOCUMENT NUMBER: 116:229469
TITLE: Cloning and expression of an A1 adenosine receptor from rat brain
AUTHOR(S): Mahan, Lawrence C.; McVittie, Loris D.; Smyk-Randall, Elizabeth M.; Nakata, Hiroyasu; Monsma, Frederick J., Jr.; Gerfen, Charles R.; Sibley, David R.
CORPORATE SOURCE: Lab. Cell Biol., Natl. Inst. Mental Health, Bethesda, MD, 20892, USA
SOURCE: Mol. Pharmacol. (1991), 40(1), 1-7
CODEN: MOPMA3; ISSN: 0026-895X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The polymerase chain reaction technique was used to selectively amplify guanine nucleotide-binding **regulatory protein** (**G protein**)-**coupled receptor** cDNA sequences from rat striatal mRNA, using sets of highly degenerate primers derived from transmembrane sequences of previously cloned **G protein-coupled receptors**. A novel cDNA fragment was identified, which exhibits considerable homol. to various members of the **G protein-coupled receptor** family. This fragment was used to isolate a full-length cDNA from a rat striatal library. A 2.2-kilobase clone was obtained that encodes a **protein** of 326 amino acids with 7 transmembrane domains, as predicted by hydropathy anal. Stably transfected mouse A9-L cells and Chinese hamster ovary cells that expressed mRNA for this clone were screened with putative receptor **ligands**. Saturable and specific binding sites for the A1 adenosine antagonist [3H]-1,3-dipropyl-8-cyclopentylxanthine were identified on membranes from transfected cells. The rank order of potency and affinities of various adenosine agonist and antagonist **ligands** confirmed the identity of the cDNA clone as an A1 adenosine receptor. The high affinity binding of A1 adenosine agonists was shown to be sensitive to the nonhydrolyzable GTP analog guanylyl-5'-imidodiphosphate. In adenylyl cyclase assays, adenosine agonists **inhibited** forskolin **stimulated** cAMP prodn. by >50%, in a **pharmacol**. specific fashion. Northern blot and in situ hybridization analyses of receptor mRNA in brain tissues revealed 2 transcripts of 5.6 and 3.1 kilobases, both of which were abundant in cortex, cerebellum, hippocampus, and thalamus, with lower levels in olfactory bulb, striatum, mesencephalon, and retina. These regional distribution data are in good agreement with previous receptor autoradiog. studies involving the A1 adenosine receptor. Thus, the cDNA cloned encodes an A1 adenosine receptor linked to the **inhibition** of adenylyl cyclase activity.

L20 ANSWER 47 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:36899 HCAPLUS
DOCUMENT NUMBER: 114:36899
TITLE: Molecular cloning and expression of a D1 dopamine

receptor linked to adenylyl cyclase activation
AUTHOR(S): Monsma, Frederick J., Jr.; Mahan, Lawrence C.; McVittie, Loris D.; Gerfen, Charles R.; Sibley, David R.
CORPORATE SOURCE: Exp. Ther. Branch, Natl. Inst. Neurol. Disord. Stroke, Bethesda, MD, 20892, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1990), 87(17), 6723-7
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In order to clone the D1 dopamine receptor linked to adenylyl cyclase activation, the polymerase chain reaction was used with highly degenerate primers to selectively amplify a cDNA seguence from NS20Y neuroblastoma cell mRNA. This amplification produced a cDNA fragment exhibiting considerable seguence homol. to guanine nucleotide-binding (G)-**protein-coupled receptors** that have been cloned previously. To characterize this cDNA further, a full-length clone was isolated from a rat striatal library by using the cDNA fragment as a probe. Sequence anal. of this cDNA clone indicated that it is induced a member of the **G-protein-coupled receptor** family and exhibits greatest homol. with the previously cloned catecholamine receptors. Northern blot anal. of various neural tissues revealed a transcript of .apprxeg.4 kb that was predominantly located in the striatum with lesser amts. in the cortex and retina. In contrast, no mRNA was detected in the cerebellum, hippocampus, olfactory bulb, mesencephalon, or pituitary. In situ hybridization anal. also revealed a high abundance of mRNA in the striatum as well as in the olfactory tubercle. To establish the identity of this cDNA, transient expression expts. were performed in COS-7 cells. [3H]SCH-23390, a D1-selective radioligand, exhibited specific, saturable binding only in cells that were transfected with this cDNA. Competition binding anal. with a variety of dopaminergic **ligands** demonstrate a D1 dopaminergic **pharmacol.** In addn., dopamine as well as other D1-selective agonists **stimulated** cAMP accumulation in transfected COS-7 cells. Therefore, the cloned cDNA encoded the D1 dopamine receptor linked to the activation of adenylyl cyclase activity.

L20 ANSWER 48 OF 48 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:546308 HCAPLUS
DOCUMENT NUMBER: 113:146308
TITLE: Cloning, functional expression, and mRNA tissue distribution of the rat 5-hydroxytryptamine1A receptor gene
AUTHOR(S): Albert, Paul R.; Zhou, Qun Yong; Van Tol, Hubert H. M.; Bunzow, James R.; Civelli, Olivier
CORPORATE SOURCE: Vollum Inst. Adv. Biomed. Res., Oregon Health Sci. Univ., Portland, OR, 97201, USA
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AB **G protein-coupled receptors** comprise a family of genes that share significant seguence similarity. A rat genomic library was screened under low-stringency hybridization conditions with the coding portion of the hamster .beta.2-adrenergic receptor gene to isolate new members of this gene family. One of these clones, clone D, codes for a 5-hydroxytryptamine1A (5-HT1A) binding site since: 1) it possesses an intronless open reading frame encoding a **protein** with 7 putative transmembrane domains and 89% amino acid

identity with the human 5-HT1A receptor (G21); 2) when transfected into Ltk- cells, it expresses a ligand-binding site with the pharmacol. of the 5-HT1A receptor subtype, including 5-HT- and spiroxatrine-displaceable binding of 8-hydroxy-(2-(N,N-di[2,3-3H])propylamino)-1,2,3,4-tetrahydronaphthalene (KH = 0.8 nM). Further, clone D encodes a functional receptor because its binding site interacts with G proteins and because it mediates agonist-induced inhibition of basal and stimulated cAMP accumulation in transfected GH4C1 pituitary cells. The tissue distribution of 5-HT1A receptor mRNA was analyzed in rat brain; 5-HT1A mRNA is present with the expected distribution of the 5-HT1A receptor (highest in septum and hippocampus) but is present as 3 RNA species (3.9, 3.6, and 3.3 kb). These studies represent the first characterization of receptor function and brain distribution of the cloned rat 5HT1A receptor.